



ROYAL SOCIETY OF MEDICINE

Vol. XLII No. 1 January 1949

## CONTENTS

|                                                                                                                       |    |
|-----------------------------------------------------------------------------------------------------------------------|----|
| Section of Obstetrics and Gynaecology                                                                                 |    |
| DISCUSSION ON EMERGENCY OBSTETRICAL SERVICE (THE FLYING SQUAD)—ITS USE AND ABUSE                                      | 1  |
| Section of Comparative Medicine                                                                                       |    |
| Host and Tissue Specificity in Infective Disease.—President's Address by Professor WILSON SMITH, M.D. . . . .         | 11 |
| Section of Pathology                                                                                                  |    |
| The Morbid Anatomist and Cancer Research.—President's Address by Professor R. W. SCARFF, M.B., F.R.S.Ed. . . . .      | 19 |
| Section of Paediatrics                                                                                                |    |
| The Present Diagnosis and Therapy of Cystic Fibrosis of the Pancreas.—DOROTHY H. ANDERSEN, M.D. . . . .               | 25 |
| Section of Odontology                                                                                                 |    |
| Orthodontic Diagnosis.—President's Address by SHELDON FRIEL, M.Dent.Sc., Sc.D., F.D.S. . . . .                        | 33 |
| Section of Urology                                                                                                    |    |
| The Ureter, the Gynaecologist and the Urologist.—President's Address by TERENCE MILLIN, M.A., M.Ch., F.R.C.S. . . . . | 37 |
| Section of Epidemiology and State Medicine                                                                            |    |
| DISCUSSION ON POLIOMYELITIS—ENGLAND AND WALES . . . . .                                                               | 47 |

(Continued on next page)



## Section of Otology

The Otologist and Rehabilitation of the Deaf.—President's Address by R. SCOTT  
STEVENSON, F.R.C.S.Ed. . . . . 55

(N.B.—The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.)

**Copyright:** The Society holds the copyright of all matter accepted for publication in the *Proceedings*. Requests for subsequent publication elsewhere should be made to the Honorary Editors. All papers, &c., presented at meetings (other than those which have been previously published) are held to be subject to the Society's copyright until a decision in regard to their publication has been made.

**Digests:** Requests for permission to make Digests from the *Proceedings* should be addressed to the Honorary Editors.

All communications concerning Editorial Business should be addressed to  
THE HONORARY EDITORS, 1, WIMPOLE STREET, LONDON, W.1

*Applications for advertisement space in the "Proceedings" should be made to the Society's official advertising agents, Messrs. C. Mitchell & Co. Ltd., Mitchell House, 1 and 2, Snow Hill, London, E.C.1.*

Copies of the whole *Proceedings* may be purchased through any bookseller. Prices are as follows:—

|                                                                  |                           |
|------------------------------------------------------------------|---------------------------|
| Single copies                                                    | 10s. 6d. each, post free. |
| Annual subscription, covering 12 monthly issues and annual index | £6 6s. 0d.                |

Reprints of Sectional parts may be obtained direct from the Society. Prices are as follows:—

|                     |                          |
|---------------------|--------------------------|
| Single copies       | 3s. 6d. each, post free. |
| Annual subscription | 15s. 0d.                 |

Fellows and Members of the Royal Society of Medicine are asked to apply direct to the Society for any copies of the *Proceedings* they may require, whether whole or Sectional, in addition to those they receive *gratis*. Prices are as follows:—

Whole *Proceedings*:

|                                                      |                          |
|------------------------------------------------------|--------------------------|
| Single copies                                        | 7s. 6d. each, post free. |
| Complete volume (12 monthly issues and annual index) | £5 0s. 0d.               |

Sectional *Proceedings*:

|                     |                          |
|---------------------|--------------------------|
| Single copies       | 3s. 0d. each, post free. |
| Annual subscription | 10s. 0d.                 |

An efficacious treatment for all forms of  
CHRONIC RHEUMATISM

# SALIODE

## GABAIL

SALIODE (Gabail) is a solution of Iodine and Salol in ether-purified Olive Oil in ampoules of 5 c.c. for intramuscular injection.

Supplied in boxes of 5 ampoules.

*Further particulars on request from*

THE ANGLO-FRENCH DRUG CO. LTD.  
11-12 GUILFORD STREET :: LONDON, W.C.1

# Section of Obstetrics and Gynæcology

President—Professor HILDA N. LLOYD, F.R.C.S., F.R.C.O.G.

[October 15, 1948]

## DISCUSSION ON EMERGENCY OBSTETRICAL SERVICE (THE FLYING SQUAD) — ITS USE AND ABUSE

Professor Hilda Lloyd (University of Birmingham): Under the new Health Act the Flying Squad service will presumably continue and at any time those of us who serve on Regional Boards or Maternity Advisory Committees may be asked for an opinion on the organization and scope of this Service.

### ORIGIN OF THE FLYING SQUAD

Under this title Newcastle upon Tyne must take the credit for starting a Service in 1935 (*see Brit. med. J.*, 1947, ii, 878).

These emergency obstetrical services sprang up in various parts of the country and no doubt their conception must have been prompted by the need of the post-partum emergency for resuscitation as well as obstetrical skill. Their tremendous growth has undoubtedly been due to their bringing both obstetrician and blood together to the patient.

Each Centre has worked out for itself the details of personnel and equipment and these have been influenced in their turn by the geographical location of the population.

For these reasons it seems opportune that we should assess the work done, and pool our experiences and lay down principles for the future working of the Service.

I have therefore undertaken a comparison between the Birmingham Emergency Service and that of Newcastle. The two areas are in complete contrast. The Birmingham Squad serves a population of over a million in the city alone and has seldom been called out to a patient more than 20 miles away; consequently cases can usually be treated within a short time of a call being received and the admission, if necessary, of a patient to hospital after treatment presents little difficulty.

The Newcastle Squad, on the other hand, serves an incomparably wider area, the distances are much greater and it has been found necessary to treat a considerable number of intra-partum emergencies in the home. Circumstances may make this necessary but it would appear scarcely desirable if it can be avoided by any means.

The statistical summary (Table I) compares the total calls in Newcastle and Birmingham between 1935 and 1948 inclusive.

| TABLE I.—STATISTICAL SUMMARY. TOTAL CALLS |             |                 |
|-------------------------------------------|-------------|-----------------|
| Year                                      | Newcastle   | Birmingham      |
| 1935                                      | 1           | Not inaugurated |
| 1936                                      | 11          | 4               |
| 1937                                      |             | 9               |
| 1938                                      |             | 25              |
| 1939                                      | 47          | 23              |
| 1940                                      |             | 22              |
| 1941                                      |             | 11              |
| 1942                                      |             | 30              |
| 1943                                      |             | 52              |
| 1944                                      |             | 73              |
| 1945                                      |             | 83              |
| 1946                                      | 56 (Record) | 116 (Record)    |
| Grand total                               | 353         | 448             |
| 1947                                      |             | 113             |
| 1948                                      |             | 58 (8 months)   |
|                                           |             | 619             |

TABLE II.—DEATHS

|                   | Newcastle<br>(353 cases to<br>1946) | Birmingham<br>(619 cases to<br>Sept. 1948) | Birmingham<br>(Last 350 cases) |
|-------------------|-------------------------------------|--------------------------------------------|--------------------------------|
| Before arrival .. | 15                                  | 9                                          | 3                              |
| After arrival ..  | 22                                  | 14                                         | 1                              |
|                   | <hr/> 37                            | <hr/> 23                                   | <hr/> 4                        |

The deaths (Table II) occurring during these years are worthy of note. Details of the 3 deaths in the last 350 cases in Birmingham are as follows: (1) Normal delivery and placenta delivered but patient died of hæmorrhage and shock. (2) Inanition and a precipitate labour—placenta delivered—no hæmorrhage and death from shock. (3) Death followed two hours after a difficult forceps delivery. The death occurring after arrival of the Squad was a case of A.P.H. and toxæmia with concealed hæmorrhage and placenta prævia. The patient died in the Maternity Hospital of anuria on the eighth day after delivery, and at post-mortem the kidneys showed the crush syndrome.

*Type of case* (Table III).—The cases in Table III show the types for which the service has been used in both places over the same number of years.

TABLE III.—TYPE OF CASE, 1935-1948

| Type of case                   | Newcastle |     | Birmingham |      |
|--------------------------------|-----------|-----|------------|------|
| Abortions and complications .. | 41        | 12% | 35         | 6%   |
| Ante-partum complications ..   | 20        | 6%  | 12         | 2%   |
| Intra-partum emergencies ..    | 45        | 13% | 10         | 1.5% |
| Immediate post-partum ..       | 231       | 66% | 550        | 89%  |
| Late post-partum ..            | 15        | 4%  | 10         | 1.5% |
| Not pregnant ..                | 1         |     | 2          |      |
|                                | <hr/> 353 |     | <hr/> 619  |      |

## EXPERIENCE GAINED BY BIRMINGHAM SQUAD

(1) *Administrative*.—(a) *Transport*: Since the inception of the service an ambulance has been used as an integral part of the team, unlike other centres which have relied upon private cars. This is a point of some importance since it allows admission to hospital without delay if the patient's condition is unsatisfactory. 192 cases were so admitted after emergency treatment, but the majority of these were in the early years before confidence had been gained in the usual smooth convalescence. In the last 350 cases only 48 were transferred, but even this proportion makes provision of an ambulance desirable. (b) *Follow-up*: During part of 1946-7 a follow-up hæmatological examination was attempted on all cases which had been transfused with blood, with satisfactory results.

(2) *Technique*.—*Transfusion*: This is often the first thing to be done even before the placenta, which may be still in the uterus, can be dealt with. The details of this and the management of the third stage of labour I am leaving to Miss Shotton to describe as she is now the officer in charge of the service.

(3) *Results*.—It is difficult to estimate the results in terms of lives saved, but it is significant that the figures for maternal mortality due to hæmorrhage in the City of Birmingham show a progressive decline during the last ten years—the period during which the Squad has been actively functioning.

For purposes of comparison I have tried to compare the last ten years (Table V) with the previous seven years, when the service was not in normal action (Table IV).

A word about the abuses of the Flying Squad: The service, as it operates in Birmingham, consists of three essential parts: the obstetrician, the resuscitation of the patient, and the transport; the obstetrician is not expected to drive the ambulance, but is expected to be a skilled resuscitation officer, and his assistants (nurse and often a student) can give him little help in this. The type of case for which the Squad was evolved—the acute post-partum emergency—needs obstetrician and resuscitation and may also need ambulance transport. It is well, however, to consider how the Squad may be abused in other types of case.

(a) *Abortion*.—Although hæmorrhage in these cases may be catastrophic the Flying Squad is an easy escape for the doctor who declines to accept the responsibility of the case. Such cases are suitable either for digital evacuation or for transfer to hospital and those which require transfusion will be very few.

TABLE IV  
Mortality rate per 1,000 live and still births due to maternal hæmorrhage

| Year    | Maternal deaths from hæmorrhage | Mortality rate per 1,000 live and still births due to maternal hæmorrhage | Total mortality rate per 1,000 live and still births |
|---------|---------------------------------|---------------------------------------------------------------------------|------------------------------------------------------|
| 1931 .. | 8                               | 0.45                                                                      | 3.66                                                 |
| 1932 .. | 9                               | 0.52                                                                      | 3.72                                                 |
| 1933 .. | 4                               | 0.26                                                                      | 3.84                                                 |
| 1934 .. | 6                               | 0.37                                                                      | 3.87                                                 |
| 1935 .. | 5                               | 0.30                                                                      | 3.52                                                 |
| 1936 .. | 12                              | 0.71                                                                      | 3.65                                                 |
| 1937 .. | 9                               | 0.51                                                                      | 3.07                                                 |
| 1947 .. | 1                               | 0.04                                                                      | 0.98                                                 |

TABLE V

| Year | Flying Squad calls | Maternal deaths from hæmorrhage | Mortality rate per 1,000 live and still births due to mat. hæmorrhage | Total mortality rate per 1,000 live and still births | Percentage deaths due to hæmorrhage |
|------|--------------------|---------------------------------|-----------------------------------------------------------------------|------------------------------------------------------|-------------------------------------|
| 1938 | 25                 | 12                              | 0.66                                                                  | 2.88                                                 | 23%                                 |
| 1939 | 23                 | 9                               | 0.50                                                                  | 2.48                                                 | 20%                                 |
| 1940 | 21                 | 4                               | 0.22                                                                  | 2.14                                                 | 11%                                 |
| 1941 | 11                 | 4                               | 0.24                                                                  | 2.43                                                 | 10%                                 |
| 1942 | 30                 | 5                               | 0.26                                                                  | 2.45                                                 | 10%                                 |
| 1943 | 52                 | 6                               | 0.29                                                                  | 1.69                                                 | 17%                                 |
| 1944 | 73                 | 3                               | 0.13                                                                  | 1.34                                                 | 10%                                 |
| 1945 | 83                 | 1                               | 0.05                                                                  | 1.41                                                 | 3%                                  |
| 1946 | 116                | 3                               | 0.13                                                                  | 0.85                                                 | 15%                                 |
| 1947 | 113                | 1                               | 0.04                                                                  | 0.98                                                 | 4%                                  |

(b) *Ante-partum emergencies.*—The majority of these will be cases of placenta prævia, and it is strongly urged that it is no part of the Flying Squad duty to go out and perform Cæsarean sections in the home. It is well known that the transport of the shocked patient is safe when transfusion is given simultaneously, and recent work has shown that without vaginal interference a patient with placenta prævia will not bleed to death.

The other ante-partum emergency to which the Squad may be called is the eclamptic, and here there is no need for a transfusion service but for transport and an obstetrician with whatever anti-convulsant therapy he favours.

(c) *Intra-partum emergencies.*—In the experience of the Newcastle Squad these cases represented 13% of the total calls, and one gets the impression that transport difficulties must have been almost insurmountable for these cases not to be dealt with by a domiciliary service. Such cases, if in need of resuscitation before delivery by the domiciliary consultant, should be transported to hospital where expert anaesthesia and full hospital facilities can be obtained. Relaxation therapy and analgesia with pethidine or trilene, &c., should tide over the patient for the journey.

(d) *Late post-partum hæmorrhage.*—These cases almost invariably require curettage after preliminary resuscitation, and the most convenient method of dealing with them is to transfer them to hospital after transfusion at home. Thus a resuscitation squad is needed rather than an expert obstetrician.

#### CONCLUSIONS

The Flying Squad's original function was to increase the safety of domiciliary midwifery, and the happy combination of obstetrician, ambulance and transfusion equipment has undoubtedly saved many lives endangered by post-partum hæmorrhage.

Demands on the service are increasing, however, and there is a real danger that the specialist obstetricians may not be sufficiently numerous to cope with all the calls.

One of the first criticisms which should be discussed is whether the expert obstetrician is possibly wasting his time when a trained transfusion officer is all that is needed.

Recently it has been noted that where a patient is thought by her doctor to require no treatment except a transfusion the Squad has been called out as there was no other means of getting blood to that patient.

Occasionally for general medical and surgical conditions this may occur and it makes one wonder whether it would be wiser to have a transfusion service run by officers expert in the technique as a separate entity from the emergency obstetrical service. I hope this criticism will be discussed by the Members.

Finally, in order that we may not wander too far from our initial objective—namely the uses and abuses of the Flying Squad—I think it would be wise if we tried to find answers to certain concrete questions, otherwise we may find ourselves wandering away from the point into the realms of management of the third stage of labour and allied subjects.

Miss Dorothy M. Shotton (Birmingham): My own experience of the Flying Squad extends over the last six years, during which time I have attended 220 cases.

When a doctor needs the Flying Squad he telephones the Maternity Hospital. Calls occasionally come in direct from midwives who cannot get a doctor, or from the ambulance service, or police. The R.S.O. receives the call and assembles the team. The hot-water bottles are filled, the blood is taken from the refrigerator, and the Flying Squad sets out. We reckon to arrive at the patient's home within half an hour of the receipt of the telephone call, provided the case is situated within the City.

*The Flying Squad team* consists of: (1) An obstetrician; (2) a nurse; (3) a student.

(1) *The obstetrician*.—At present we have six in a rota, three obstetric surgeons, two registrars, and the R.S.O. of the Maternity Hospital. This type of work demands considerable obstetric experience, as well as skill in resuscitation work. It is eminently a job for the junior consultant. There is possibly scope for a resuscitation officer, but in my opinion it is essential that an obstetrician should be in charge. Here are two illustrative cases in support of this contention. On both occasions the doctor stated that the third stage of labour was complete, but that the patient required a transfusion. In both cases I gave blood, but the patient failed to respond. In the first case I found that the cord had been pulled off the placenta and delivered, together with a blood clot, the placenta being left behind in the uterus. I removed the placenta, after which the patient's condition improved. In the second case a vaginal examination revealed the uterus completely inverted and lying in the vagina. It was not until the uterus was replaced that recovery took place. If a resuscitation officer alone had been called to these cases it is probable that the obstetric condition would have been overlooked.

The surgeon in charge of the Flying Squad is responsible for organizing the rota, for receiving complaints and suggestions, and for the general maintenance of equipment.

(2) *The nurse*.—We have a rota of staff midwives on call day and night, who know every detail of the apparatus and are responsible for seeing that the equipment is in order when they return from the case. One senior nurse checks over the apparatus each month.

(3) *The student*.—One of the resident midwifery students goes on each call, both to learn and also to give practical help.

*The transport*.—The Flying Squad is transported by ambulance, one being kept always in readiness at the ambulance depot. The advantages of this means of transport are three-fold: (a) The patient can be transported to hospital if necessary. (b) The equipment is too bulky to go with ease into the average-sized car. (c) The ambulance always knows the way, and can get through the traffic quickly.

The obstetrician, however, particularly as he becomes adept at finding his way about the town, often finds it easier to go direct in his own car.

*The equipment* consists of:

- |                                                     |                                    |
|-----------------------------------------------------|------------------------------------|
| 1 Holdall containing blankets and hot-water bottles | 2 Insulated boxes containing blood |
| 3 Leather bags                                      | 1 Telescopic blood stand           |
| 2 Sterile drums                                     | 1 Oxygen cylinder                  |

The contents of the three leather bags are as follows:

| General                                             |                                  |
|-----------------------------------------------------|----------------------------------|
| Mackintosh aprons and sheet                         | Selection of bowls               |
| Splint, bandages, strapping                         | Sphygmomanometer and stethoscope |
| Ministry of Health needle and cannula giving sets   | Glass funnel and rubber tubing   |
| Sterile syringes, needles and catgut, in containers | Head lamp and hand lamp          |
| Sterile packet of dressings and galley pots         | Lithotomy strap                  |
| Bag of masks                                        | Distilled water                  |
|                                                     | Antiseptics                      |
|                                                     | Nail brush and soap              |
|                                                     | Tin of biscuits for the staff    |

*Anæsthetic Materials*

Ether  
Chloroform  
Pentothal  
Bag of anæsthetic apparatus

*Drugs*

|                |            |
|----------------|------------|
| Morphia        | Pitocin    |
| Phenobarbitone | Methyldine |
| Atropine       | Cocaine    |
| Ergometrine    | Procaine   |

*Resuscitation fluids carried are:*

3 pints blood. Group O. Rh positive  
 3 pints blood. Group O. Rh negative  
 2 pints dried plasma  
 1 pint glucose saline

*Instruments*

Artery forceps, scissors, needle holder,  
 dissecting forceps, sponge forceps,  
 volsellum forceps, ovum forceps,  
 curette, vaginal speculum, obstetric  
 forceps, catheters

One sterile drum contains a gown, towels, swabs, pads and a gauze pack; the other contains a sterile cutting-down set, towels and swabs. There is also a box of sterilized gloves.

There is a duplicate of the entire equipment, so that we can answer two calls at once if necessary.

The purpose of the Flying Squad is to deal with cases of hæmorrhage and shock associated with pregnancy. In other cases of abnormal labour it is much better that an obstetrician should go out alone and either deal with the case or have it transferred to hospital, as he thinks fit.

In this type of work there are bound to be a certain number of unnecessary calls. In the last 300 cases there have only been 19 in which no treatment was required—a proportion of 6%, which seems fairly reasonable.

*The management of the case.*—On arrival at the patient's house we take a brief history from the doctor or midwife and then proceed to a rapid examination of the patient. In determining whether or not a transfusion is required, the three great signs are: (a) The blood-pressure; (b) the pulse-rate; (c) the patient's general condition—her colour and behaviour, and the evidence of loss of blood.

Of these three, the blood-pressure is the most reliable sign, though very grave signs are air-hunger, failing vision, and a restless unco-operative patient.

Abdominal examination reveals the condition of the uterus.

The cases can roughly be divided into three classes:

(a) *The borderline case*, in which there is time to consider whether resuscitation is required or not.

(b) This class constitutes the majority of cases. The patient is considerably shocked, with a systolic blood-pressure of 70 or less. She is generally not bleeding. The abdomen is tender from repeated manipulations of the uterus. This case obviously needs resuscitation urgently, and definitely before any operative procedure or removal to hospital is attempted.

(c) In a few cases the patient is at death's door. Blood-pressure and pulse are unrecordable, and panic reigns. A transfusion must be started within two or three minutes, and often run in under positive pressure.

From the moment of arrival the student is detailed to take a ten-minute record of the blood-pressure and pulse-rate, and to keep a record of all treatment given on a special chart. In cases in which the placenta is already expelled, it is mainly a matter of administering resuscitation, though a sluggish uterus often has to be dealt with by catheterization, or giving ergometrine. We also repair any lacerations that may be present.

*Resuscitation.*—Blood is given immediately, usually by a needle into an arm vein, occasionally by cutting down. We give Group O blood, without grouping or cross-matching the patient. The reason for this is that we feel that to group the patient, though a simple procedure, is not devoid of error, particularly when done in a hurry. If a mistake were made, and a large volume of, say, Group A blood were given in error to a Group B patient, the result would be disastrous. In order to be really certain, cross-matching of the blood is essential, and this, to be done accurately, takes half an hour. We therefore prefer to rely on Group O blood, and personally I have never seen an immediate reaction. If the patient is known to be Rh-positive we give Rh-positive blood, but if there is any doubt, Rh-negative blood is given. We have always had great help from the Regional Blood Transfusion Service in obtaining a bank of Group O Rh-negative blood.

As more patients are grouped ante-natally, we hope to be able to take blood of the correct group to the patient. As an extra precaution we try, when possible, to give the first few ounces of blood slowly, and we make it a rule to give as little blood as possible, and only when really necessary. Plasma is now very seldom given, on account of the risk of homologous serum jaundice.

Other treatments for shock are given, as well as blood. Morphia is excellent, and during the last two and a half years we have been giving methyline if the blood-pressure is still low when the blood volume has been restored. This gives very good results.

The average amount of blood given is two pints. We aim at leaving the patient in good condition, with a systolic blood-pressure of 100, and a pulse-rate of less than 112.

*The removal of the placenta.*—The best time to do this is as soon as the patient shows signs of improvement—usually within twenty minutes of starting the transfusion, when half to one pint of blood has been given. I believe that retention of the placenta adds to the shock, either by the presence of a contraction ring, or by repeated small hæmorrhages, and that, therefore, the sooner the placenta is removed, the better. I never give ergometrine before the delivery of the placenta, because it makes the subsequent manual removal more difficult. The anæsthetic used is pentothal, which can easily be given by the student into the drip. The minimum dose is given, often only 0.25 gram. I leave the patient as she lies in the bed, for any movement adds to the shock. I never attempt a Credé's expression, but proceed straightaway to a manual removal. Contraction rings always respond to the inhalation of amyl nitrite. In the last three and a half years I have done 73 cases by this method, and in every case the patient's condition at the end of the operation has been better than at the start.

*The disposal of the case.*—We have an arrangement with five local hospitals to admit any case that we think requires removal to hospital, but there is an increasing tendency to leave the patient at home. In 1944, 41% of the cases were transferred to hospital—in 1947 only 17%. We ask the patient's own doctor to visit her and give her iron, but the prophylactic use of sulphonamides or penicillin is not advised. We ask the doctor to let us know if pyrexia occurs, and I know of only one case that had to be admitted to hospital on this account.

As we leave the house we always ask the husband to see that his wife has her next baby in hospital.

*Cases of abortion and ante-partum hæmorrhage* are best transferred to hospital. We give enough resuscitation to make the ambulance journey safe, in bad cases often keeping the blood drip going throughout the journey. The systolic pressure should be 100 before it is safe to move the patient, as a drop of 20 may be expected during transit.

Miss Josephine Barnes (University College Hospital, London): The Flying Squad at University College Hospital has been in operation since 1938 but the number of cases has been many fewer than those experienced by Birmingham and work of this kind in London came virtually to a standstill during the recent war. We have, however, been able to come to certain definite conclusions as the result of our experience of this type of work. These may be summarized as follows:

The maternity Flying Squad must really "Fly". This requires thorough organization and everyone concerned, including telephone operators, ambulance staff and medical and nursing staff, must be fully conversant with the routine and must know their own roles thoroughly. This applies to the regular staff and to any relief staff.

Equipment must be adequate. Since 1946 rhesus-negative blood has always been used unless the mother is known to be rhesus positive. In the past human serum has been extensively used but in view of the danger of hepatitis we shall restrict its use in the future, preferring to use saline.

An ambulance is a great asset, not only to carry bulky equipment but also to transport the patient to hospital if her condition permits. In the conditions prevailing in London we find it preferable to admit the patient to hospital whenever possible. Home conditions are generally bad in the districts we serve and the distance to the hospital is never great.

Nevertheless we believe that the Flying Squad does useful work and that it is a service that should be organized on a nation-wide basis. We are greatly indebted to the Blood Transfusion Service who are maintaining regular supplies of blood under difficulties. We always ask the patient's husband to enrol as a blood donor and to persuade his friends to do the same as a return for the treatment, in most cases involving blood transfusion, received by his wife.

Dr. David Shaw (Manchester): *Résumé.*—No one doubts the value of the Flying Squad for certain obstetrical emergencies, and our aim should be to organize a midwifery service so that an emergency unit is available for every woman in labour throughout the country. But it is equally certain that no stereotyped organization should be forced upon us, and that each centre and surrounding district should be allowed to develop independently, as it is clear from the Discussion that a service designed for a large country district would be of little use in London or the large provincial cities.

The results show, I think, the efficacy of placing one well-trained resident in sole charge of the service, who soon acquires considerable experience in this type of work; attends a sufficient number of cases each year to assess new ideas and methods; becomes himself an experienced hæmatologist in constant touch with advances in this new branch of medicine; reduces delay to a minimum, and thereby increases the service's effective range.

The use of ergometrine in controlling third-stage hæmorrhage—apart entirely from true post-partum hæmorrhage—has been learnt in quite recent times, and deserves the attention of all practising obstetricians.

A large proportion of these emergency cases, I feel certain, result from mismanagement of the third stage of labour in normal cases, and when this becomes abnormal for one reason or another, from abortive attempts at placenta delivery.

The Manchester City Emergency Maternity Unit was founded in 1938 by the Medical Officer of Health for the city, who wisely left the administration in the hands of my hospital, the only large, then voluntary, maternity unit in the district.

In 1946 I became, what I believe to be, the first wholtime Flying Squad Officer in Great Britain, answering practically every call myself for six months.

TABLE I.—RESULTS

| Year          | Total calls | Deaths |
|---------------|-------------|--------|
| 1938          | 9           | 2      |
| 1939          | 9           | 1      |
| 1940          | 13          | 0      |
| 1941          | 16          | 1      |
| 1942          | 18          | 0      |
| 1943          | 20          | 2      |
| 1944          | 63          | 1      |
| 1945          | 59          | 3      |
| 1946          | 77          | 1      |
| 1947          | 149         | 2      |
| 10 year total | 433         | 13     |

Table I shows the total calls and deaths for each year; it should be noted that since the introduction of the wholtime officer in January 1947, the number of deaths has not increased, although the number of calls has almost doubled.

TABLE II.—COMPARISON OF TYPE OF CASE TREATED BY NEWCASTLE AND MANCHESTER EMERGENCY SERVICES

| Stabler's classification | Newcastle | Manchester |
|--------------------------|-----------|------------|
| Immediate post-partum    | 231       | 231        |
| Intra-partum             | 45        | 11         |
| Ante-partum              | 20        | 10         |
| Abortions                | 41        | 12         |
| Late P.P.H.              | 15        | 6          |
| Not pregnant             | 1         | 4          |

In Table II, I have collected for each Squad consecutive cases until each group contained 231 immediate post-partum complications. A glance shows the relatively large number of cases attended in Newcastle, classified in groups other than "immediate post-partum". It would therefore appear that the Newcastle Unit has a practice differing somewhat from our own. We regard the Squad's work as largely confined to the first group of case—immediate post-partum—with selected cases of abortion and ante-partum hæmorrhage. Obstetrical emergencies in labour, of which we have our fair share, are not considered as Flying Squad work, the majority of whom can be safely transported to, and more efficiently treated in, hospital.

In recent years most of our patients have remained in their own homes for subsequent treatment, which I feel certain is partly responsible for our low mortality. This point I should like to stress, as it is a lesson that has been learnt from bitter experience: in the early days many cases were transported to hospital and there died.

My personal cases fall naturally into three groups: first, abnormal third stage, secondly, true post-partum hæmorrhage, and thirdly, a group containing all other conditions.



TABLE III.—ANALYSIS OF 155 CALLS—1946, 1947 (JANUARY TO JUNE)

| Group I                  | Group II     | Group III              |
|--------------------------|--------------|------------------------|
| Retained placenta<br>107 | P.P.H.<br>25 | Other conditions<br>23 |
| Total calls ..           | ..           | 155                    |
| Deaths ..                | ..           | 3                      |

Table III shows the three groups; it only remains for me to point out that all three deaths occurred in Group I, which contains two-thirds of all the cases treated. For these reasons my thoughts and efforts have been mainly directed to this group.

TABLE IV.—RETAINED PLACENTAS

|                                      |     |
|--------------------------------------|-----|
| Total calls ..                       | 107 |
| Placenta delivered before arrival .. | 33  |
| Placenta delivered by Squad ..       | 74  |
| 1. Manual removal ..                 | 57  |
| 2. Crêdè expression ..               | 4   |
| 3. Oxytocic drug ..                  | 11  |
| 4. Spontaneous ..                    | 1   |
| 5. Not removed ..                    | 1   |

Table IV analyses the 107 cases of Group I—third-stage complications. Thirty-three placentas were delivered in one way or another by a doctor or midwife before arrival of the Squad; although many of these cases required resuscitation by the Squad, in the majority the emergency had passed and the patient's condition was improving. On the whole these patients were in better condition than those whose placentas were still retained. There is no doubt that timely intervention, before a patient's condition has deteriorated from blood loss and shock, is preferable to abortive attempts to deliver the placenta which only shocks the patient; she then requires a blood transfusion before the placenta can be safely delivered.

This is not the time to discuss the third stage of labour, but I must pass comment upon the eleven placentas successfully delivered by an intravenous oxytocic drug—usually ergometrine. In this small series it considerably reduced the incidence of manual removal, with its attendant risk of a general anæsthetic to an ill woman.

I also wish to record that, for the abnormal third stage, a large number of cases have been ordered an oxytocic drug by the Flying Squad Officer before leaving the hospital, to be given by the doctor intravenously or the midwife intramuscularly. In only a few cases is the placenta delivered when the Squad arrives, but in a considerable number the uterus has contracted down upon the retained placenta and prevented further bleeding. It is my impression that, employed in this fashion, ergometrine has a definite part to play in arresting third-stage hemorrhage, and thereby maintaining a patient's condition until the arrival of the emergency unit.

To anticipate criticism, I may say that in no case have I encountered a contraction ring. A Bandl's ring is usually present for a time, but gradually disappears, or may be dilated manually without difficulty.

Mr. Alistair Gunn (London County Council) described the scope of action, equipment, organization and personnel of the Emergency Obstetric Service in London and gave some of the results in South-East London.

He paid a tribute to Dr. Letitia Fairfield who organized the service in 1939 for three teaching hospitals to undertake responsibility for one-fifth of the London area, and for L.C.C. hospitals to provide emergency obstetric units for the other four-fifths. His own two hospitals serve the south-east quarter of London with a population of 800,000 and about 14,000 annual births. A doctor in London who needs the service telephones the patient's name and address to the London Ambulance Service which immediately sends an ambulance to the hospital nearest the address. The ambulance service meanwhile telephones the hospital to have the obstetrician, a trained nurse, the equipment and stored blood ready for the ambulance to pick up at the hospital gates.

Mr. Gunn said that during nine years working in London the Flying Squads had rarely found it necessary to carry out any operative procedure other than the immediate resuscitation of the patient and the injection of drugs, such as morphia and ergometrine, with a view to the removal of the patient to hospital. This was the chosen plan because the calls were all within 5 miles of fully equipped obstetric units. It was necessary to send an experienced

obstetrician if all the lives possible were to be saved. Most of the 55 cases in South-East London in the past three years had been in a critical condition and only 2 had died.

The Flying Squads from St. Alfege's Hospital, Greenwich, and Lewisham Hospital used blood transfusion extensively, starting with Rhesus-negative Group O blood, while a sample of blood was sent to the laboratory for the resident pathologist to Rhesus test, group and cross-match with blood while the messenger waited. The present supply of plasma had been reported to give a high incidence of infective jaundice, and so plasma transfusion had been suspended.

Mr. Anthony W. Purdie (London) described the emergency obstetric service available at the North Middlesex Hospital to practitioners in the neighbourhood, and showed lantern slides illustrating its salient features. 123 cases had been attended from 1938 until the end of September 1948.

This was an urban service. Its greatest value was in the treatment of serious post-partum hæmorrhage. In 87% of the cases of post-partum hæmorrhage attended transfusion of whole blood had been administered. Transfusion of gum-saline, serum and plasma had been abandoned early in the series.

He advised the practitioner to give morphine and ergometrine while waiting for the obstetrician to arrive. He considered that after the obstetrician's arrival in the patient's house, the best results were to be obtained by the rapid transfusion of blood (under pressure from a bellows if necessary) followed by manual removal of the placenta under general anaesthesia given by the practitioner. He considered it a decided mistake to move the seriously ill patient to hospital.

He agreed with those speakers who considered that an obstetrician should be in charge of this mobile service. In urban practice, at any rate, he favoured simplicity in personnel. He himself went alone with his equipment by car or ambulance, and relied upon the general practitioner and midwife in attendance for assistance.

Mr. Frank Stabler (Newcastle): There are several points I wish to make. First, on a point of historical importance I must correct our Chairman for we were not the first service in Britain. Bellshill in Lanarkshire preceded us by some months. Secondly, I must emphasize strongly that it is very wrong to compare our service with any so far mentioned in this Discussion. To compare and contrast figures in services of this nature is completely valueless. We serve an area one hundred miles in extent. Many of our cases are in isolated farmsteads up in the hills or in pit villages many miles away. Others are in small country maternity homes. The effect of distance is that transport to hospital is often not to be thought of whereas in a city like Birmingham it may well be the best policy. This accounts for the comparatively large number of intrapartum emergencies we have dealt with. When it is said that such cases as placenta prævia are best brought into hospital I would reply that many of our cases are already in a maternity unit albeit a small country affair. Professor Lloyd said that secondary post-partum hæmorrhage was an example of a condition which could always be brought into hospital. Only a month ago I was called 25 miles to a woman eight days delivered who had what I think is a record low blood-pressure—a systolic of 34 mm. Hg. She had a retained cotyledon of placenta and made a good recovery.

Another reason why our record should not be put against those of other centres is that it is quite obvious to me that our cases are much more serious than any that have been presented to-night. With a population half of that we serve, Professor Lloyd has had twice the number of calls. It follows either that our practitioners are omitting to call us when they should or that the Birmingham service is attending three patients out of four which would not be considered serious enough in our district. Of course I approve of practitioners sending for the less serious cases but this does make any comparison of results valueless. The London records I have seen at this meeting show long sequences of patients with blood-pressure of 100 or more and pulse-rate 80 which to us would not appear to justify calling on the Emergency Service.

On the problem of personnel I feel very strongly that an obstetrician, and a senior obstetrician at that, is essential. There are often major obstetric problems to be decided where skill and experience make all the difference. Miss Shotton asked whether a resuscitation officer should be included in the team. I think this is an unnecessary complication and indeed the knowledge and skill necessary to be expert at resuscitation can quickly be acquired by any obstetrician.

We always use Group O Rhesus-negative blood and had the importance of this brought home to us by losing a patient from an incompatible transfusion when we relied on

information supplied by the medical officer of the small hospital in which the emergency had arisen.

Our total of cases in thirteen years has now risen to 500 (*see Brit. med. J.*, 1947, ii, 878). In the last 147 cases we have had three deaths after treatment was instituted and three were dead on arrival.

The three main points I wish to make are: (1) that the service in our district is not comparable with any other I know of; (2) that it is essential to have the attendance of an expert obstetrician; (3) that if a case is fit to transport to hospital it is not a case for the Emergency Service at all.

Further details of the services at St. Alfege's Hospital, Greenwich, and Lewisham Hospital were given by Dr. Catherine Blyth and Dr. J. Karnicki respectively.

Mr. A. P. Bentall (Norwich) saw the danger of the Squad becoming too elaborate and put in a plea for chloroform as an anaesthetic rather than pentothal.

Mr. W. G. Mills (Birmingham) gave it as his opinion that the Flying Squad should be replaced by an association between an Emergency Resuscitation Service in charge of the Regional Transfusion Officer, and an obstetrician. In some cases, as outlined above, the Resuscitation team alone would be needed, while in the majority of the post-partum emergencies the obstetrician would attend to remove the placenta and give reassurance, and would be free to depart elsewhere while the transfusion was competently concluded.

Other speakers included Dr. D. N. Struan Robertson (Oxford), Miss Letitia Fairfield (London), Professor J. Chassar Moir (Oxford), Dr. G. Roworth (Swindon), and Dr. Muriel Rose (Edware).

## Section of Comparative Medicine

President—Professor WILSON SMITH, M.D.

[October 20, 1948]

### Host and Tissue Specificity in Infective Disease

#### PRESIDENT'S ADDRESS

By Professor WILSON SMITH, M.D.

UNSOLVED problems of specificity meet us in whatever bacterial or virus infection we choose to investigate. The fact that one animal species is susceptible and another resistant to a certain micro-organism may seem too obvious to cause surprise, but how little we know of the factors involved! Why does the leprosy bacillus infect only man whilst the bovine tubercle bacillus causes natural infection in many species and can be experimentally imposed upon several more? Is it because *M. lepræ* requires some essential growth factor to be found only in human tissue? Then what are we to make of the similar host specificity of the gonococcus which can grow outside the body on a variety of artificial culture media? Or of the fact that of two neurotropic viruses, one, like that of poliomyelitis, has only one natural host whilst another, like that of rabies, has several. In some cases racial differences within a single species seem to be more important than species differences; for example Algerian sheep are said to be resistant to anthrax which is a disease not only of other breeds of sheep but also of bovines, pigs and man. Even within a race individuals may show curious and inexplicable differences of susceptibility. Most of us have envied the fortunate individual who never catches a cold and my experience with experimental virus infections of mice convinces me that such individual resistance, quite apart from any question of acquired immunity, is a very real thing. The work of Webster (1937) in breeding bacteria-resistant and virus-resistant strains of mice from the same original stock indicates that genetic constitution determines such behaviour, but in saying this we are merely begging the question and are still left with the problem of what genetic factors affect susceptibility behaviour and the manner in which they function.

Similar anomalies exist in respect of the attack of an infective organism on the host's tissues. In view of the close relationship between the gonococcus and the meningococcus their tissue predilections are somewhat curious. I have often wondered why gonococci are never found in the nasopharynx and meningococci never in the urethra for there is no lack of opportunity for transfer to the sites in question. One of the most striking examples of the interplay of host and tissue specificities is afforded by experimental tuberculosis in the rabbit and guinea-pig, and one has the feeling that if we knew the fundamental reasons for the characteristic distributions of lesions in these species we would be a good step nearer to control of the human disease. Even within a single organ tissue specificity may be apparent. For example Lovell and Cotchin (1946) found that *C. renale*, inoculated intravenously in mice, attacked the kidney medulla to the exclusion of the cortical tissue whilst in influenza it is only certain types of cells in the respiratory tract which suffer the virus invasion.

These few examples serve to illustrate the complexity of the problems arising from the specificity of host-parasite interactions. They also indicate the close inter-relationship between host and tissue specificities. In some cases the former may be entirely conditioned by the latter. For example, if the virus of encephalitis lethargica requires for its growth a metabolite or an enzyme only to be found in certain cells of the human central nervous system it is clear that the disease must remain always a specific human infection. Indeed, in the last analysis, host susceptibility must always be dependent upon the ability of host cells to participate in biochemical reactions conjointly with either the infecting organism or

its products. The converse, however, by no means follows, for the isolated cells of a completely resistant host species may be fully capable of promoting bacterial or virus growth and may even show in tissue culture the characteristic signs of specific infection. Also the susceptibility of the tissues of an animal may be readily demonstrable by experimental infection although the species never contracts the disease in nature. One may therefore distinguish between the specificity determined by the susceptibility or non-susceptibility of cells as cells, irrespective of their environment within the host, and that determined by the host or tissue resistance which results from environmental and extrinsic factors, in spite of the susceptibility of constituent cells.

#### EXTRINSIC FACTORS IN HOST SPECIFICITY

These extrinsic factors are numerous and some, like portal of entry, participation of ecto-parasites, presence of bactericidal agents such as lysozyme, &c., are relatively easy to understand. Others are more complex and invite further experimental investigation. Consider the factor of host body temperature. In some few cases the effect may well be a direct one depending upon the temperature range for growth of the micro-organism in question. This may account for much of the species specificity of the gonococcus and *Treponema pallidum*, a hypothesis deriving some support from the results of pyrotherapy in neurosyphilis. But no such simple explanation will suffice in other cases. *B. anthracis* has a fairly wide temperature range, yet the importance of body temperature in susceptibility to anthrax is strikingly illustrated by the susceptibility of chickens immersed in cold water and of frogs maintained at 35° C. Recent work by Cromartie and his collaborators (1947) suggests that species resistance to anthrax is bound up with failure of capsulation *in vivo* and it may be that, with many other pathogens also, the metabolism of some aggressin-like constituent requires a much finer adjustment of temperature than *in vitro* cultivation would suggest.

It is a common assumption that animals at the extremes of age and in a poor state of nutrition are particularly susceptible to bacterial and virus infections. This is often true and may be readily explained on the basis of relative inefficiency of the normal defence reactions. But the reverse also is often true so that, as in rinderpest or foot-and-mouth disease, it is the well-nourished young adults which contract the infection and succumb. One can scarcely postulate here that a relative inefficiency of the normal defence reactions is responsible. One imagines that the speed and vigour of cellular metabolism may be concerned. The exceptional growth capacity of embryonic tissue is assumed to favour the reproduction of some viruses and it is equally feasible that others may require a balance of cellular metabolites only attained in the slower metabolism of adult healthy tissues. The necessity of using well-nourished healthy guinea-pigs for eliciting satisfactory skin reactions to diphtheria toxin accords well with this hypothesis.

The importance of bacterial exotoxins in the initiation of some infections and their effect upon the subsequent distribution and localization of lesions are too well known to require emphasis. Much less is known about the effect of metabolic products which exert no direct toxic action but may none the less influence both the host and tissue specificities of a micro-organism. One of the most striking examples is afforded by staphylococci. Here a normal body mechanism, the clotting of fibrinogen, which is of extreme importance in the defence of the host against injury, is adapted by the staphylococcus for its own protection against the host's defence reactions. Hale and I (1945) were able to demonstrate experimentally that the coagulase activity of staphylococci results in an aggregation of the organisms in a matrix of fibrin clot and that in such situation the microbes are relatively resistant to the attack of phagocytic cells. The fact that species differ in respect of their plasma coagulability suggested that staphylococcal species specificity might be largely determined by this activity. Further experiments lent support to this view for we were able to produce infections in normally resistant species by supplying the missing coagulable substrate (Smith *et al.*, 1947). Recent work has shown that the coagulase activities of staphylococci are much more complex than were originally thought. There are undoubtedly many coagulases or at least modifications of the coagulase structure reflected in a variability in the range of host plasmas clotted by different strains. Furthermore, mutation of staphylococcal strains associated with a change of coagulase activity occurs not infrequently. There is thus provided a mechanism whereby the host specificity of a micro-organism may change and it is probable that the many strains of staphylococci with different host specificities now existing derived from a single progenitor strain.

Host resistance is so closely bound up with acquired immunity and the production of the serum antibodies, upon which such immunity so largely depends, that the possible significance of normal antibody-like substances as a factor in species specificity tends to be overlooked. Indeed so obsessed are we by the doctrines of immunology that any protective

power of a normal serum is usually attributed to the presence of so-called normal antibodies with the assumption that these have been produced like true immune bodies in response to specific antigenic stimuli. Without in any way denying that this does occur I suggest that similar constituents of serum and tissue fluids exist, entirely independently of specific antigenic stimuli, and that these constitute one factor in the species specificities of some infective agents. The so-called non-specific inhibition of influenza hæmagglutination by many normal sera is a well-known phenomenon and McCrea (1946) produced evidence that normal serum globulin is concerned. In recent studies with my colleague, Miss Westwood, I have been surprised at the very high hæmagglutinin neutralizing titres of sera obtained from animals which could not possibly have had previous contacts with the virus, and in unpublished work we have obtained indications that lipids or lipid protein complexes may be sometimes responsible and that species differ greatly in their content of such substances. It is difficult to avoid the conclusion that substances capable of reacting with virus receptors must be a factor in susceptibility or resistance to the virus. Failure to demonstrate a virus neutralization effect by *in vivo* animal tests is in no way proof to the contrary, for the artificial introduction of test doses of virus into highly susceptible experimental animals introduces factors which are absent from the host-parasite relationships in the field. In the case of normal ferret sera, however, such *in vivo* neutralization has been demonstrated both in mice and in chick embryos and quite recently we have obtained striking neutralization of influenza virus with guinea-pig serum in the usual type of mouse neutralization test.

Time does not allow discussion of the many other extrinsic factors though some of them like diet, sex, physiological characteristics of certain tissues and species peculiarities of anatomical structure possess points of special interest. More fundamental still are the specificity factors which I propose to call intrinsic because they determine the susceptibility or non-susceptibility of cells, as cells, irrespective of their organization into tissues or of the extrinsic factors arising from their environment.

#### INTRINSIC CELLULAR SUSCEPTIBILITY

Some light has been shed upon mechanisms involved in this intrinsic cell specificity by recent researches in several different fields; most notably from the investigations concerned with virus hæmagglutination, with the bacteriophages, with interference phenomena and with virus adaptability to different hosts. All these researches concern chiefly the viruses. This emphasis on virus-cell interaction rather than on bacterial invasion is natural because the virus reacts as a unit, entering the host cell and multiplying therein whereas in the case of bacteria this is seldom so. As Dubos (1945) says: "Specificity is no longer referred to the bacterial cell as a whole; it is the summation of the multiple specificities of the many components and attributes of the cell." While attention is directed here chiefly to virus infections it must be borne in mind that similar mechanisms of specific reactions are almost certainly utilized by bacterial components and bacterial products.

(a) *Virus hæmagglutination*.—In 1941 Hirst first reported the phenomenon of virus hæmagglutination. He found that chick red blood cells aggregated into clumps when brought into contact with influenza virus. It was soon recognized that this was no isolated phenomenon. The erythrocytes of some other species were found to be agglutinable and several other viruses were found to possess hæmagglutinating activity. For example, human red cells are agglutinated not only by all known types and strains of influenza virus but also by the viruses of mumps and Newcastle disease of fowls whilst mouse cells remain unaffected by these viruses but are clumped by ectromelia virus. It is thus obvious that specific attractions occur between the erythrocytes of many species and certain viruses. The cellular aggregation depends first upon a union of virus particles to cell surface but analogy with serological agglutination would suggest that for aggregation to follow such union both virus and cell must be multivalent so that the virus may act as a bridge between cells. That mouse cells are unaffected by influenza virus is not strictly true for whilst the cells fail to agglutinate they do adsorb the virus, suggesting that the specific cell receptors fall below the critical level required for the formation of a lattice. Again, in terms of serological reactions, one may postulate that many viruses are monovalent, like haptens, so that they can never cause agglutination of cells to which they become united. For infectivity, however, cell agglutination is of no importance; the essential reaction is union between parasite and cell. Such specific linkage is probably necessary for the development of the chain of subsequent cell-virus interactions involved in the infective process. In the case of influenza we are able to study one of the subsequent reactions. A short time after the red cells have agglutinated, dissociation of the complex occurs with elution of the virus from the cell surface. The eluted virus is, by all known criteria, unchanged but the cell cannot be re-agglutinated by the same virus because it has lost its specific receptors. Although heat-killed virus can agglutinate erythrocytes it is unable to initiate this stage of elution because the heat treatment has destroyed a virus enzyme concerned in the reaction. The probability

its products. The converse, however, by no means follows, for the isolated cells of a completely resistant host species may be fully capable of promoting bacterial or virus growth and may even show in tissue culture the characteristic signs of specific infection. Also the susceptibility of the tissues of an animal may be readily demonstrable by experimental infection although the species never contracts the disease in nature. One may therefore distinguish between the specificity determined by the susceptibility or non-susceptibility of cells as cells, irrespective of their environment within the host, and that determined by the host or tissue resistance which results from environmental and extrinsic factors, in spite of the susceptibility of constituent cells.

#### EXTRINSIC FACTORS IN HOST SPECIFICITY

These extrinsic factors are numerous and some, like portal of entry, participation of ecto-parasites, presence of bactericidal agents such as lysozyme, &c., are relatively easy to understand. Others are more complex and invite further experimental investigation. Consider the factor of host body temperature. In some few cases the effect may well be a direct one depending upon the temperature range for growth of the micro-organism in question. This may account for much of the species specificity of the gonococcus and *Treponema pallidum*, a hypothesis deriving some support from the results of pyrotherapy in neurosyphilis. But no such simple explanation will suffice in other cases. *B. anthracis* has a fairly wide temperature range, yet the importance of body temperature in susceptibility to anthrax is strikingly illustrated by the susceptibility of chickens immersed in cold water and of frogs maintained at 35° C. Recent work by Cromartie and his collaborators (1947) suggests that species resistance to anthrax is bound up with failure of capsulation *in vivo* and it may be that, with many other pathogens also, the metabolism of some aggressin-like constituent requires a much finer adjustment of temperature than *in vitro* cultivation would suggest.

It is a common assumption that animals at the extremes of age and in a poor state of nutrition are particularly susceptible to bacterial and virus infections. This is often true and may be readily explained on the basis of relative inefficiency of the normal defence reactions. But the reverse also is often true so that, as in rinderpest or foot-and-mouth disease, it is the well-nourished young adults which contract the infection and succumb. One can scarcely postulate here that a relative inefficiency of the normal defence reactions is responsible. One imagines that the speed and vigour of cellular metabolism may be concerned. The exceptional growth capacity of embryonic tissue is assumed to favour the reproduction of some viruses and it is equally feasible that others may require a balance of cellular metabolites only attained in the slower metabolism of adult healthy tissues. The necessity of using well-nourished healthy guinea-pigs for eliciting satisfactory skin reactions to diphtheria toxin accords well with this hypothesis.

The importance of bacterial exotoxins in the initiation of some infections and their effect upon the subsequent distribution and localization of lesions are too well known to require emphasis. Much less is known about the effect of metabolic products which exert no direct toxic action but may none the less influence both the host and tissue specificities of a micro-organism. One of the most striking examples is afforded by staphylococci. Here a normal body mechanism, the clotting of fibrinogen, which is of extreme importance in the defence of the host against injury, is adapted by the staphylococcus for its own protection against the host's defence reactions. Hale and I (1945) were able to demonstrate experimentally that the coagulase activity of staphylococci results in an aggregation of the organisms in a matrix of fibrin clot and that in such situation the microbes are relatively resistant to the attack of phagocytic cells. The fact that species differ in respect of their plasma coagulability suggested that staphylococcal species specificity might be largely determined by this activity. Further experiments lent support to this view for we were able to produce infections in normally resistant species by supplying the missing coagulable substrate (Smith *et al.*, 1947). Recent work has shown that the coagulase activities of staphylococci are much more complex than were originally thought. There are undoubtedly many coagulases or at least modifications of the coagulase structure reflected in a variability in the range of host plasmas clotted by different strains. Furthermore, mutation of staphylococcal strains associated with a change of coagulase activity occurs not infrequently. There is thus provided a mechanism whereby the host specificity of a micro-organism may change and it is probable that the many strains of staphylococci with different host specificities now existing derived from a single progenitor strain.

Host resistance is so closely bound up with acquired immunity and the production of the serum antibodies, upon which such immunity so largely depends, that the possible significance of normal antibody-like substances as a factor in species specificity tends to be overlooked. Indeed so obsessed are we by the doctrines of immunology that any protective

cells. The development of resistance to lysis therefore may be due either to loss of surface receptors or alternatively to the masking of specific receptors by the development of new surface components. A point of special significance is the fact that extracted receptor substance may block phage action so that extracts of bacteria, or even the purified polysaccharide of a specific antigen, will prevent lysis when added to the mixtures of phage and bacteria. Has this any significance for the study of the host-parasite relationship in man and animals? I think that it has. The virus neutralization effects of so-called non-specific inhibitory substances of normal sera have already been mentioned. One of these inhibitors is almost certainly derived from red cell receptors for a polysaccharide with closely similar activity can be extracted from human group O erythrocytes. It is therefore not difficult to imagine that susceptible tissue cells shed off similar receptor substances which can interfere with the first stage of cell parasitization by viruses. One might even postulate that the relative insusceptibility of young animals to some infections may be due to the more active discharge of such substances by cells which have a brisker metabolism than those of susceptible adults.

Bacteriophage studies have shown clearly that the highly specific union of phage to bacterial cell occurring at spatially distinct receptor spots on the cell surface is an absolutely essential preliminary to the further reactions leading to lysis. The blockage of receptors with inactivated phage renders the microbe resistant to fully active phage. Such blockage has analogies in serological reactions and is almost certainly the basis of the interference phenomenon encountered in several human and animal virus infections. This phenomenon was first recorded by Hoskins in 1935; he found that monkeys inoculated with a neurotropic strain of yellow-fever virus were protected against the lethal effects of a pantropic strain inoculated simultaneously or even previously. It was soon established that similar effects were demonstrable with other viruses, that inactivated virus might interfere with living virus and that cross interference between serologically unrelated viruses might occur. The cellular basis of the phenomenon was established by Andrewes (1942) who demonstrated it in tissue cultures. Such interference effects are more closely connected with problems of individual acquired resistance than with species and tissue specificities but the facts do reinforce the conclusion derived from haemagglutination work that in some cases these specificities depend upon the surface configurations of body cells. If the receptors of a micro-organism happen to correspond with rare cellular configurations to be found only in one species, or in one type of cell, then the parasite will exhibit the strictest specificity in respect of host or tissue or both.

Bacteriophage studies have revealed a most remarkable quantitative aspect of the interference phenomenon which demands some explanation other than the simple blockade of cell receptors and which I feel must have a bearing upon specificity problems. It is clear from both adsorption experiments and electron microscopy that a bacterium may specifically adsorb as many as two hundred phage particles; yet only one of them is destined to infect the cell, multiply therein, and produce cell lysis. Infection by one particle prevents in some way entry of the remainder. More than this, it may prevent infection by other phages. Luria and Delbrück (1943) suggest that the interference is due to competition for a key enzyme of the bacterial cell, present in such small amount that it may be deviated by even a single unit of inactivated phage.

A hypothesis accepted by some authorities states that the life-long immunity which follows certain virus diseases depends upon persistence of undetectable virus in tissue cells. Other authorities refute this on the ground that tissue cells have a limited span of life and that the *pari passu* growth and division of cells and virus, required for such a perfect symbiotic relationship, is inconceivable. In the bacteriophages, however, we have many examples of just such a state of affairs. The lysogenic strains of bacteria carry phages to which they themselves are resistant, and in the case of sporing bacteria, the phages are transmitted to daughter cells arising from the spores. To quote Topley and Wilson (1946): "In the carrier state represented by a lysogenic strain it is clear that the multiplication of phage and bacterium must be so co-ordinated that when a bacterium divides each daughter cell receives its quota of phage." Moreover, lysogenicity is often acquired by bacteria as a result of their experimental infection with a phage and this involves permanent future resistance against the phage in question and, may be, against some closely related phages also. The work of Williams Smith (1948) indicates that similar changes probably occur in nature. If such perfectly adjusted symbiosis can be acquired by bacteria, why not also by animal tissue cells? Indeed, there is some evidence that this does occur. There are many carriers of herpes virus but only when extraneous factors upset the symbiosis do signs of the infection appear. The same virus of herpes has been shown to survive in the rabbit brain for as long as nine months after recovery from infection (Good, 1947). There are many other examples of such prolonged survival of various viruses in the tissues after recovery from infection.



that elution depends upon enzymic destruction of a cell surface substrate was suggested by Hirst in his original paper but it is to Burnet and his many collaborators that we owe most of our knowledge of the nature of the reactions concerned (Burnet *et al.*, 1946). The virus enzyme is closely related to a mucinase easily extracted from *V. cholerae*. This cholera mucinase destroys red cell receptors in exactly the same way as do the viruses, and both cholera enzyme and viruses can be shown to have similar activities on various other mucinous substrates. There is thus clear proof that many viruses possess enzymes, similar to a bacterial enzyme, which can break down host tissue substrates, quite apart from the intracellular reactions associated with virus multiplication. The remarkable specificity of the reactions is illustrated by Burnet's work on what he terms the receptor gradient of human red cells. Viruses of the influenza group can be arranged in a linear series of increasing activity so that the interaction of any member with human erythrocytes leaves the cells still agglutinable by viruses coming later in the series but not re-agglutinable by the same virus or any of those preceding it in the series (Burnet *et al.*, 1946). The significance of these facts is very hard to evaluate but the phenomena of the receptor gradient, and of certain interference effects between viruses of this group and cholera enzyme which there is not time to discuss, are incompatible with the theory of specific receptors for each type of virus or of spatially distinct receptors with different degrees of availability for different viruses. Stone (1947) therefore postulates a single complex cell receptor for all the viruses of the influenza group in which progressive degrees of degradation can occur.

We thus have a picture of specific linkage of cell and parasite by means of corresponding receptors as a preliminary to a specific biochemical reaction at the cell surface. These interactions in the case of red blood cells would seem to be entirely without influence on the infection process because, so far as we know, in none of the diseases mentioned are the erythrocytes concerned. I am not yet convinced of this, however, and as a pure speculation suggest that the linkage and subsequent elution offer a beautiful mechanism for the speedy removal of virus from the circulation and its transference to depots for destruction.

Be that as it may, we now have clear experimental proof that identical reactions occur between virus and tissue cells which are susceptible to infection and, moreover, that the reactions are essential constituents of the infection process. As early as 1943 Hirst demonstrated the adsorption of influenza virus by some of the pulmonary cells during perfusion of the excised ferret lung with virus fluids, and also the spontaneous elution of the adsorbed virus after a short time. Similar perfusion experiments were carried out by Fazekas de St. Groth (1948) in mice. He had the advantage of being able to apply the knowledge gained by Burnet in respect of cholera enzyme. The lung cells readily adsorbed either living or killed virus but whereas a large percentage of adsorbed living virus was subsequently eluted the killed virus never did so unless freed by means of cholera enzyme. Preliminary perfusion of the lungs with the enzyme prevented any subsequent virus adsorption because of the destruction of the cell receptors. Subsequently Stone (1948) carried out a beautiful series of experiments in fertile hen eggs where the susceptible cells, like those of the ferret and mouse lungs, can be shown first to adsorb inoculated virus and then elute it. Briefly, the preliminary treatment of the eggs with cholera enzyme prevents subsequent virus adsorption and also, in consequence, prevents infection. It appears probable that with the influenza group of viruses the destruction of the cell receptors by the virus enzyme may be necessary for the virus penetration of the cell. Whether the eluted virus represents the excess which fails to penetrate, whether as in the case of some bacteriophages and human spermatozoa cell penetration by one particle renders the cell impermeable to others, we do not know. In the egg receptor regeneration occurs but only after an interval of several days and it is easy to see the part which this mechanism may play in the transient immunity associated with some infections like the common cold.

(b) *Bacteriophage studies.*—Researches on bacteriophages have given further clues to the mechanisms of intrinsic cellular specificity in infective disease. The host ranges of different phages vary widely; some of them attack whole groups of organisms whilst others are strictly specific. Indeed, as Dubos (1945) puts it: "Specificity is so narrow that it is defined in terms of strains of bacteria rather than species and even variant forms of one strain." In most cases the essential factor in determining the susceptibility of a group of organisms to a single phage appears to be the possession of a common antigenic component; for example, one phage is able to lyse *S. typhi*, *S. enteritidis* and *S. pullorum* which share the group antigens IX and XII. The S→R variation of some bacterial species may be associated with loss of susceptibility to one phage but acquirement of susceptibility to another which happens to require the availability of an R antigen. It is well known, of course, that the different phage types of *Vi* strains of *S. typhi* show no detectable serological differences but no one would be bold enough to suggest that antigenic components detectable by our available serological techniques are the only receptor substances at the surfaces of bacterial

(1) Adaptation to one new host species may prepare the way for subsequent adaptation to a second. Thus, as in the case of influenza virus, adaptations may fall into a progressive series. I am aware that some strains of this virus have been isolated from human cases by direct egg inoculation but there is no doubt that egg and mouse infections are more likely to succeed with ferret-adapted virus than with human material.

(2) Adaptation is usually accompanied by loss of original characters as well as by acquisition of new ones. Virulence for the primary host usually declines and may be completely lost. This fact, of course, forms the basis of many successful methods of immunization.

(3) The adaptation to a new host may involve adaptation to a new tissue. Cases in point are the neurotropism of mouse yellow-fever virus and the neurotropic strain of influenza virus already mentioned.

(4) Whilst the mutation of an organism in respect of one single character is probably a sudden discontinuous phenomenon, adaptation to a new host is often gradual. This suggests that progressive mutation of one character or mutations of several associated characters are involved.

(5) Different strains of the same virus differ in the ease with which they can be adapted to a new host. Mouse adaptation of ferret strains of influenza virus may be easy or may require prolonged serial passage before signs of mouse infection can be obtained.

(6) Adaptation may or may not be associated with a demonstrable change of antigenic constitution. Burnet's O and D phases of egg-adapted influenza virus show strikingly different haemagglutination behaviour but may be indistinguishable by serological and cross immunity tests (Burnet, 1943). On the other hand, Hirst (1947) found that two antigenically identical strains from an epidemic deviated on mouse passage to produce antigenically distinct derivative strains and also that each derivative strain differed from its own parent strain.

(7) Acquisition of power to parasitize a new host's tissue does not necessarily confer power to cause disease. Hirst (1947) demonstrated this clearly by adapting an egg strain of influenza virus to mice and estimating the virus content of the mouse lungs at each passage by egg titrations. The virus multiplied to full titre in the mouse lungs right from the outset but its power to produce lung lesions and to kill mice rose slowly.

It seems to me that these conclusions, together with some of the phenomena of haemagglutination and bacteriophage action which I have discussed, are incompatible with the conception of multitudinous stable receptor groups, spatially distinct on the surfaces of tissue cells and viruses or with the conception of host susceptibility being dependent upon some specific moiety of a virus which can be quantitatively increased or decreased, or even completely lost. We have seen that with many viruses cell infection depends initially upon linkage with or adsorption on the cell. This is only to say that a certain degree of closeness of apposition is required before biochemical reactions between enzymes and substrates can proceed and I suggest that such apposition is the primary infection factor with all viruses. Thus, provided that the cells contain suitable substrates and enzymes, intrinsic cell susceptibility will be entirely determined by the molecular configurations of cell and virus surfaces. The association of a virus with its natural host, apart, of course, from the many important extrinsic factors which can affect the issue, must have been occasioned originally by a chance similarity or "complementariness" of surface configurations. If so the strict host-specificity of some viruses and the wide range of animal species parasitized by others are not surprising.

Perhaps this is merely presenting the receptor theory in different form but the postulation of relative non-specificity and plasticity of the surface configuration of a virus provides an explanation of the phenomena of virus adaptability. I suggest that the mechanism of such adaptations is closely akin to the mechanism of specific antibody production. There is little doubt that antibodies are produced by cells which originally had the function of manufacturing normal serum globulins or that antibody molecules differ from normal globulin molecules only in peculiarities of surface configuration. Whatever may be the relative validities of the various modern theories of the way in which this is brought about, the certain fact remains that the stimulus of an antigen upon the globulin-forming cells results in a re-orientation of cell activity which persists long after the antigenic stimulus is withdrawn and which, moreover, is transmissible to daughter cells through many generations. This antibody-forming cell is just as much a mutant as the egg-adapted strain of influenza virus or the neurotropic yellow-fever virus. If, then, the configuration of the antigenic components of a microbe can determine the direction of cell mutation and thereby the configuration of the globulin molecules being synthesized, it is surely more than likely that the surface configurations of tissue cells will effect similar changes in organisms which once

If one accepts the possibility that man and animals may enjoy the perfectly adjusted cell virus symbiosis shown by lysogenic bacteria there can be no difficulty in accepting the further probability that such association will have results more far-reaching than the maintenance of homologous immunity. Much more fundamental would be a resultant cellular resistance against both homologous and heterologous virus infections based upon the key enzyme competition postulated by Luria and Delbrück (1943). This might be a factor not only in individual immunity but also in species non-susceptibility. We know very little about the aetiology of the frequent minor pyrexial disturbances of infancy. May not some of them be virus infections leaving behind a legacy of cell-virus symbiosis which serves as a barrier against later infection with other known viruses? In view of the very early colonization of the intestine with a characteristic normal bacterial flora, which undoubtedly plays an important part in the maintenance of health, is it not conceivable that a normal virus flora of the tissues exists which must remain undetected until techniques for the recognition of non-pathogenic viruses have been evolved?

(c) *Adaptability of viruses.*—One of the most fascinating aspects of the host-parasite relationship is the remarkable adaptability of some viruses to new host species and to new types of tissue. It is axiomatic that a living organism is capable of adaptation to environment but the adaptations we are concerned with involve much more than mere temporary behaviour; they require structural and functional alterations of more or less permanent nature and constitute what we term mutation. The potentialities for mutation vary widely with different pathogenic micro-organisms and are probably partly dependent upon their size and complexity of structure. Some few viruses are almost, if not quite, non-adaptable to any new host whilst others adapt very readily. It is probable that all the viruses originally had a strict specificity for a single host species but the evolutionary trend is always towards multiplication of derivative strains by mutation with consequent extension of the range of host species susceptible to infection. Such natural adaptations, however, are bound to be very infrequent, being dependent upon chance concatenations of favourable circumstances, but by artificial experimental infection the progression of mutations can be speeded up enormously.

The first isolation of influenza virus required the use of the ferret. Previously there must have been hundreds of abortive attempts to infect various species by inoculations of human material. Now consider what has happened to the original strain since its primary isolation. The ferret disease was readily transmissible in series and although the impunity with which sick animals could be handled suggests that some loss of virulence of the virus for man must have occurred, there is fairly conclusive evidence of the contraction of human infection from a ferret of the 196th passage (Smith and Stuart-Harris, 1936). Further adaptation to the mouse was first achieved with ferret material of the 166th passage but production of a highly virulent mouse strain took many passages through mice and was accompanied by some decline of infectivity for the ferret and probably further reduction of virulence for man. From the ferret also adaptations to guinea-pig and rat were carried out but in both these species the infections remained symptomless: a striking demonstration of the fact that multiplication of a disease agent within a host does not of itself necessarily cause disease. From mouse lung, virus was transmitted to the chorio-allantoic membrane of the chick embryo and from the membrane adaptation to the amnion was achieved. Finally, a natural adaptation to chick embryo brain tissue occurred during egg membrane passage which enabled Stuart-Harris (1939) to evolve a neurotropic strain, pathogenic for mice with the production of a fatal encephalitis on intracerebral inoculation.

Before considering the implications of these changes I wish to refer to the work of Dr. J. T. Edwards with quite a different virus, that of rinderpest. This virus is a natural pathogen for cattle but is virtually non-pathogenic for goats. Edwards was able to obtain strains virulent for the goat by serial passage through this species and the adaptation was accompanied by a steady decline of virulence for cattle. Different races of oxen have different thresholds of susceptibility but for a single race Edwards believes that it is possible to obtain virus of any desired degree of virulence by subjecting it to different numbers of passages through goats. The fully adapted goat virus is naturally infective for goats, that is to say inoculated animals can pass on the infection to other goats by contact. In a similar manner rinderpest virus can be adapted to rabbits, again with decline of virulence for the original host species. To explain such behaviour Edwards has postulated that the virus contains different moieties each of which is concerned with the infectivity for a particular animal species so that by adaptative passage one moiety is increased at the expense of the others. This conception is, of course, similar to the theory of specific cell receptors to account for hæmagglutination phenomena.

There are numerous other examples of virus mutation, many of which possess features of special interest, but from the behaviour of the two viruses of influenza and rinderpest it is possible to draw certain conclusions of fairly general applicability:

(1) Adaptation to one new host species may prepare the way for subsequent adaptation to a second. Thus, as in the case of influenza virus, adaptations may fall into a progressive series. I am aware that some strains of this virus have been isolated from human cases by direct egg inoculation but there is no doubt that egg and mouse infections are more likely to succeed with ferret-adapted virus than with human material.

(2) Adaptation is usually accompanied by loss of original characters as well as by acquisition of new ones. Virulence for the primary host usually declines and may be completely lost. This fact, of course, forms the basis of many successful methods of immunization.

(3) The adaptation to a new host may involve adaptation to a new tissue. Cases in point are the neurotropism of mouse yellow-fever virus and the neurotropic strain of influenza virus already mentioned.

(4) Whilst the mutation of an organism in respect of one single character is probably a sudden discontinuous phenomenon, adaptation to a new host is often gradual. This suggests that progressive mutation of one character or mutations of several associated characters are involved.

(5) Different strains of the same virus differ in the ease with which they can be adapted to a new host. Mouse adaptation of ferret strains of influenza virus may be easy or may require prolonged serial passage before signs of mouse infection can be obtained.

(6) Adaptation may or may not be associated with a demonstrable change of antigenic constitution. Burnet's O and D phases of egg-adapted influenza virus show strikingly different hæmagglutination behaviour but may be indistinguishable by serological and cross immunity tests (Burnet, 1943). On the other hand, Hirst (1947) found that two antigenically identical strains from an epidemic deviated on mouse passage to produce antigenically distinct derivative strains and also that each derivative strain differed from its own parent strain.

(7) Acquisition of power to parasitize a new host's tissue does not necessarily confer power to cause disease. Hirst (1947) demonstrated this clearly by adapting an egg strain of influenza virus to mice and estimating the virus content of the mouse lungs at each passage by egg titrations. The virus multiplied to full titre in the mouse lungs right from the outset but its power to produce lung lesions and to kill mice rose slowly.

It seems to me that these conclusions, together with some of the phenomena of hæmagglutination and bacteriophage action which I have discussed, are incompatible with the conception of multitudinous stable receptor groups, spatially distinct on the surfaces of tissue cells and viruses or with the conception of host susceptibility being dependent upon some specific moiety of a virus which can be quantitatively increased or decreased, or even completely lost. We have seen that with many viruses cell infection depends initially upon linkage with or adsorption on the cell. This is only to say that a certain degree of closeness of apposition is required before biochemical reactions between enzymes and substrates can proceed and I suggest that such apposition is the primary infection factor with all viruses. Thus, provided that the cells contain suitable substrates and enzymes, intrinsic cell susceptibility will be entirely determined by the molecular configurations of cell and virus surfaces. The association of a virus with its natural host, apart, of course, from the many important extrinsic factors which can affect the issue, must have been occasioned originally by a chance similarity or "complementariness" of surface configurations. If so the strict host-specificity of some viruses and the wide range of animal species parasitized by others are not surprising.

Perhaps this is merely presenting the receptor theory in different form but the postulation of relative non-specificity and plasticity of the surface configuration of a virus provides an explanation of the phenomena of virus adaptability. I suggest that the mechanism of such adaptations is closely akin to the mechanism of specific antibody production. There is little doubt that antibodies are produced by cells which originally had the function of manufacturing normal serum globulins or that antibody molecules differ from normal globulin molecules only in peculiarities of surface configuration. Whatever may be the relative validities of the various modern theories of the way in which this is brought about, the certain fact remains that the stimulus of an antigen upon the globulin-forming cells results in a re-orientation of cell activity which persists long after the antigenic stimulus is withdrawn and which, moreover, is transmissible to daughter cells through many generations. This antibody-forming cell is just as much a mutant as the egg-adapted strain of influenza virus or the neurotropic yellow-fever virus. If, then, the configuration of the antigenic components of a microbe can determine the direction of cell mutation and thereby the configuration of the globulin molecules being synthesized, it is surely more than likely that the surface configurations of tissue cells will effect similar changes in organisms which once

If one accepts the possibility that man and animals may enjoy the perfectly adjusted cell virus symbiosis shown by lysogenic bacteria there can be no difficulty in accepting the further probability that such association will have results more far-reaching than the maintenance of homologous immunity. Much more fundamental would be a resultant cellular resistance against both homologous and heterologous virus infections based upon the key enzyme competition postulated by Luria and Delbrück (1943). This might be a factor not only in individual immunity but also in species non-susceptibility. We know very little about the aetiology of the frequent minor pyrexial disturbances of infancy. May not some of them be virus infections leaving behind a legacy of cell-virus symbiosis which serves as a barrier against later infection with other known viruses? In view of the very early colonization of the intestine with a characteristic normal bacterial flora, which undoubtedly plays an important part in the maintenance of health, is it not conceivable that a normal virus flora of the tissues exists which must remain undetected until techniques for the recognition of non-pathogenic viruses have been evolved?

(c) *Adaptability of viruses.*—One of the most fascinating aspects of the host-parasite relationship is the remarkable adaptability of some viruses to new host species and to new types of tissue. It is axiomatic that a living organism is capable of adaptation to environment but the adaptations we are concerned with involve much more than mere temporary behaviour; they require structural and functional alterations of more or less permanent nature and constitute what we term mutation. The potentialities for mutation vary widely with different pathogenic micro-organisms and are probably partly dependent upon their size and complexity of structure. Some few viruses are almost, if not quite, non-adaptable to any new host whilst others adapt very readily. It is probable that all the viruses originally had a strict specificity for a single host species but the evolutionary trend is always towards multiplication of derivative strains by mutation with consequent extension of the range of host species susceptible to infection. Such natural adaptations, however, are bound to be very infrequent, being dependent upon chance concatenations of favourable circumstances, but by artificial experimental infection the progression of mutations can be speeded up enormously.

The first isolation of influenza virus required the use of the ferret. Previously there must have been hundreds of abortive attempts to infect various species by inoculations of human material. Now consider what has happened to the original strain since its primary isolation. The ferret disease was readily transmissible in series and although the impunity with which sick animals could be handled suggests that some loss of virulence of the virus for man must have occurred, there is fairly conclusive evidence of the contraction of human infection from a ferret of the 196th passage (Smith and Stuart-Harris, 1936). Further adaptation to the mouse was first achieved with ferret material of the 166th passage but production of a highly virulent mouse strain took many passages through mice and was accompanied by some decline of infectivity for the ferret and probably further reduction of virulence for man. From the ferret also adaptations to guinea-pig and rat were carried out but in both these species the infections remained symptomless: a striking demonstration of the fact that multiplication of a disease agent within a host does not of itself necessarily cause disease. From mouse lung, virus was transmitted to the chorio-allantoic membrane of the chick embryo and from the membrane adaptation to the amnion was achieved. Finally, a natural adaptation to chick embryo brain tissue occurred during egg membrane passage which enabled Stuart-Harris (1939) to evolve a neurotropic strain, pathogenic for mice with the production of a fatal encephalitis on intracerebral inoculation.

Before considering the implications of these changes I wish to refer to the work of Dr. J. T. Edwards with quite a different virus, that of rinderpest. This virus is a natural pathogen for cattle but is virtually non-pathogenic for goats. Edwards was able to obtain strains virulent for the goat by serial passage through this species and the adaptation was accompanied by a steady decline of virulence for cattle. Different races of oxen have different thresholds of susceptibility but for a single race Edwards believes that it is possible to obtain virus of any desired degree of virulence by subjecting it to different numbers of passages through goats. The fully adapted goat virus is naturally infective for goats, that is to say inoculated animals can pass on the infection to other goats by contact. In a similar manner rinderpest virus can be adapted to rabbits, again with decline of virulence for the original host species. To explain such behaviour Edwards has postulated that the virus contains different moieties each of which is concerned with the infectivity for a particular animal species so that by adaptive passage one moiety is increased at the expense of the others. This conception is, of course, similar to the theory of specific cell receptors to account for haemagglutination phenomena.

There are numerous other examples of virus mutation, many of which possess features of special interest, but from the behaviour of the two viruses of influenza and rinderpest it is possible to draw certain conclusions of fairly general applicability:

## Section of Pathology

President—Professor R. W. SCARFF, M.B., F.R.S.Ed.

[October 19, 1948]

### The Morbid Anatomist and Cancer Research

#### PRESIDENT'S ADDRESS

By Professor R. W. SCARFF, M.B., F.R.S.Ed.

CANCER research has tended to become very much divided into specialized fields, and there is a danger that the main problem may be lost sight of in a maze of detail. In investigating the fundamental nature of cancer it is obvious that much specialized work has to be done, and such work is being actively pursued in many directions. It is to these investigations that we must look for the ultimate solution of the problem but it is not generally realized that in this field there still remains a great deal to be done by the morbid anatomist using ordinary naked-eye and microscopical methods. Much of the work is on the clinico-pathological side and, in this, real co-operation between the clinician and the pathologist is of the greatest value. There is, however, a considerable amount concerned purely with the investigation of cancer, and the morbid anatomist can provide information that may be extremely valuable to those carrying out more detailed and more specialized investigations. His part does not end merely with diagnosing the condition present and giving it a name, nor with trying to suggest a primary site responsible for a secondary deposit. Essential though this is, he can go much further and make contributions in other directions, amongst which may be mentioned:

- (1) The recognition of conditions likely to give rise to cancer.
- (2) The correlation of histological appearances with behaviour.
- (3) Research into the nature of cancer.

(1) *The recognition of conditions likely to give rise to cancer.*—The term "pre-cancerous" seems for some reason to be under a cloud but there is no objection to its use provided one knows its meaning; it should be used to denote any condition of the tissue in which malignancy is more likely to occur than in normal tissue. There are a large number of conditions which fall into this class and many are still being debated.

In the breast atypical proliferation of the epithelium must be regarded as a danger sign and, although disputed by many, there is an increasing weight of evidence in favour of the likelihood of its progression to carcinoma. The evidence has been confused up till now by consideration of a number of retrogressive and degenerative conditions together with the epithelial proliferations. Bulk assessment of these will naturally enough not give any information. Even when one has separated off from the general mass of material the conditions in which there is overgrowth of epithelium further subdivision is still necessary, as Mrs. E. K. Dawson (1943) has shown and has distinguished by the terms *adenosis* and *epitheliosis*. There are all degrees of epithelial overgrowth and there is evidence accumulating that retrogression is possible with many of these, but that a point can be reached beyond

obtain sufficient closeness of apposition to permit the occurrence of biochemical interactions. I believe that the conception of plasticity of molecular configuration, with transmissibility of acquired adaptative forms, is capable of extension to the further reactions which occur after a virus has entered the cell and also to reactions between cell substrates and bacterial enzymes. Thus, serial passage through a new host species will result not only in the selective survival of chance mutants best fitted for the new environment but also in progressive adaptations of molecular configurations to give ever-increasing closeness of fit. This will necessarily entail distortion of the original patterns upon which depended the susceptibility of the primary host and as a consequence there will be a decline of virulence of the parasite for this primary host species. Adaptations of this sort would obviously open up possibilities of further adaptations to yet other species possessing cell patterns still more unlike those of the primary host. Re-acquisition of original characters would be based upon the same sequence of progressive adaptations but in reverse order.

In conclusion I would like to pay a tribute to the pioneer investigator in this field of research, Paul Ehrlich. Whatever we know, or think we know, about the mechanisms of host and tissue specificity in infective disease is based upon foundations laid by his work or the work of those who were stimulated by his imaginative conceptions.

Were Ehrlich here with us to-day I fear he would offer searching criticisms of the theories I have put before you. But I am confident that he would fully endorse the sentiment with which I wish to close: theory requires test—speculation must be followed by experiment.

#### REFERENCES

- ANDREWES, C. H. (1942) *Brit. J. exp. Path.*, 23, 214.  
 BURNET, F. M. (1943) *Med. J. Aust.*, 1, 385.  
 —, MCCREA, J. F., and STONE, J. D. (1946) *Brit. J. exp. Path.*, 27, 228.  
 —, and ANDERSON, S. G. (1946) *Brit. J. exp. Path.*, 27, 236.  
 CROMARTIE, W. J., BLOOM, W. L., and WATSON, D. W. (1947) *J. infect. Dis.*, 80, 1.  
 DUBOS, R. J. (1945) *The Bacterial Cell*. Harvard Univ. Press, Cambridge, Mass.  
 FAZEKAS DE ST. GROTH, S. (1948) *Aust. J. exp. Biol. med. Sci.*, 26, 29.  
 GOOD, R. A. (1947) *Proc. Soc. exp. Biol. N.Y.*, 64, 360.  
 HALE, J. H., and SMITH, W. (1945) *Brit. J. exp. Path.*, 26, 209.  
 HIRST, G. K. (1941) *Science*, 94, 22.  
 — (1943) *J. exp. Med.*, 78, 99.  
 — (1947) *J. exp. Med.*, 86, 357.  
 HOSKINS, M. (1935) *Amer. J. trop. Med.*, 15, 675.  
 LOVELL, R., and COTCHIN, E. (1946) *J. comp. Path.*, 56, 205.  
 LURIA, S. E., and DELBRÜCK, M. (1943) *Arch. Biochem.*, 1, 207.  
 MCCREA, J. F. (1946) *Aust. J. exp. Biol. med. Sci.*, 24, 283.  
 SMITH, H. W. (1948) *J. Hyg., Camb.*, 46, 82.  
 SMITH, W., HALE, J. H., and SMITH, M. M. (1947) *Brit. J. exp. Path.*, 28, 57.  
 —, and STUART-HARRIS, C. H. (1936) *Lancet* (ii), 121.  
 STONE, J. D. (1947) *Aust. J. exp. Biol. med. Sci.*, 25, 137.  
 — (1948) *Aust. J. exp. Biol. med. Sci.*, 26, 49.  
 STUART-HARRIS, C. H. (1939) *Lancet* (i), 497.  
 TOPLEY, W. W. C., and WILSON, G. S. (1946) *Principles of Bacteriology and Immunity*, Third Edition. London.  
 WEBSTER, L. T. (1937) *J. exp. Med.*, 65, 261.

As with many arguments that are sustained for a long time, it is possible that all the contestants are right in individual instances. There are cases of epithelial overgrowth which show no tendency to become malignant, cases which show an increased tendency to malignancy and cases, as postulated by Muir, which are already malignant although still within the duct. In the separation of these cases we are largely relying on impression, but it should be possible to collect sufficient evidence to allow us to distinguish the three types.

Other examples can be given both in glands and in epithelial surfaces of well-known pre-cancerous conditions; these include proliferative changes in intestinal mucosa, in prostate, in skin, tongue, cervix and so on. Newcomb (1933) has shown that peptic ulceration plays a small but definite part in the ætiology of carcinoma of the stomach.

(2) *Correlation of histological appearance with behaviour. The grading of carcinoma.*—It is unfortunate that controversy has arisen with regard to the grading of carcinoma. This has been engendered by exaggerated claims of mathematical precision on the one hand and on the other hand a distrust of any numerical notation. It is to be regretted that such an issue has blinded the eyes of many to the real increase in knowledge that can be obtained by histological assessment of malignancy. There is no need to neglect the elementary, but none the less fundamental, factors of anaplasia, evidence of rapid growth, &c., in considering any type of carcinoma, and considerable benefit may come from an assessment of what the worker is actually accomplishing by means of grouping or grading. It is, of course, desirable to compare the histology and clinical course of individual cases, but such a process would be too complicated to give any result, so that one is forced arbitrarily to divide cases into groups for purposes of comparison; but if one bears in mind that these groups are merely convenient lengths cut off a graduated scale there is no objection to numbering them as grades. This grading is, of course, particularly valuable if one, at the same time, is able to pay attention to the stage the disease has reached. The sort of result obtained is seen in Table I for carcinoma of the

TABLE I

| Grade |                      | Percentage survival |          |
|-------|----------------------|---------------------|----------|
|       |                      | 5 years             | 10 years |
| I     | Low malignancy early | 80                  | 65       |
| III   | High malignancy late | 3                   | 3        |

breast (Patey and Scarff, 1928; Scarff and Handley, 1938; Truscott, 1947). For the sake of clarity intervening grades and stages are omitted; it does not matter if Grade I is called histological low malignancy and Stage I early clinical spread. Figures are merely a convenience and as long as this is appreciated there is no harm in their use. The fact that grading may not be entirely successful may be of considerable importance and give rise to new knowledge. In the case cited here of the breast we have not 100% survival in Grade I, Stage I. There are several explanations of this, one of which has received much attention—that is, that there may be unsuspected paths of early spread, and in fact it was this result that led Handley and Thackray (1947) to investigate the internal mammary chain as a route of spread, hitherto only considered to be involved late in the disease. Their striking results have shown that the internal mammary chain may be involved without any involvement of the axillary lymphatic glands. At the other end of the scale the fact that Grade III, Stage III—or, if preferred, high malignancy with advanced spread—do not show 100% death within ten years also requires some explanation; it may indicate that in this small percentage the growth has been eradicated before it has gone beyond the line of operation, or it may be an indication of a development of some systemic resistance which we will consider later on.

Another disability is the fact that growths of similar histological appearances and



which retrogression is unlikely. I am suggesting that in figs. 1 and 2 there is a dangerous degree of epithelial overgrowth which has not yet reached the irreversible carcinoma stage. In figs. 3 and 4 I would suggest that this is definitely an intra-duct carcinoma, as described by Muir (1941), and that time alone would determine frank malignancy.



FIG. 1.  $\times 35$ .



FIG. 2.  $\times 250$ .



FIG. 3.  $\times 50$ .



FIG. 4.  $\times 250$ .

As with many arguments that are sustained for a long time, it is possible that all the contestants are right in individual instances. There are cases of epithelial overgrowth which show no tendency to become malignant, cases which show an increased tendency to malignancy and cases, as postulated by Muir, which are already malignant although still within the duct. In the separation of these cases we are largely relying on impression, but it should be possible to collect sufficient evidence to allow us to distinguish the three types.

Other examples can be given both in glands and in epithelial surfaces of well-known pre-cancerous conditions; these include proliferative changes in intestinal mucosa, in prostate, in skin, tongue, cervix and so on. Newcomb (1933) has shown that peptic ulceration plays a small but definite part in the aetiology of carcinoma of the stomach.

(2) *Correlation of histological appearance with behaviour. The grading of carcinoma.*—It is unfortunate that controversy has arisen with regard to the grading of carcinoma. This has been engendered by exaggerated claims of mathematical precision on the one hand and on the other hand a distrust of any numerical notation. It is to be regretted that such an issue has blinded the eyes of many to the real increase in knowledge that can be obtained by histological assessment of malignancy. There is no need to neglect the elementary, but none the less fundamental, factors of anaplasia, evidence of rapid growth, &c., in considering any type of carcinoma, and considerable benefit may come from an assessment of what the worker is actually accomplishing by means of grouping or grading. It is, of course, desirable to compare the histology and clinical course of individual cases, but such a process would be too complicated to give any result, so that one is forced arbitrarily to divide cases into groups for purposes of comparison; but if one bears in mind that these groups are merely convenient lengths cut off a graduated scale there is no objection to numbering them as grades. This grading is, of course, particularly valuable if one, at the same time, is able to pay attention to the stage the disease has reached. The sort of result obtained is seen in Table I for carcinoma of the

TABLE I

| Grade |                      | Percentage survival |          |
|-------|----------------------|---------------------|----------|
|       |                      | 5 years             | 10 years |
| I     | Low malignancy early | 80                  | 65       |
| III   | High malignancy late | 3                   | 3        |

breast (Patey and Scarff, 1928; Scarff and Handley, 1938; Truscott, 1947). For the sake of clarity intervening grades and stages are omitted; it does not matter if Grade I is called histological low malignancy and Stage I early clinical spread. Figures are merely a convenience and as long as this is appreciated there is no harm in their use. The fact that grading may not be entirely successful may be of considerable importance and give rise to new knowledge. In the case cited here of the breast we have not 100% survival in Grade I, Stage I. There are several explanations of this, one of which has received much attention—that is, that there may be unsuspected paths of early spread, and in fact it was this result that led Handley and Thackray (1947) to investigate the internal mammary chain as a route of spread, hitherto only considered to be involved late in the disease. Their striking results have shown that the internal mammary chain may be involved without any involvement of the axillary lymphatic glands. At the other end of the scale the fact that Grade III, Stage III—or, if preferred, high malignancy with advanced spread—do not show 100% death within ten years also requires some explanation; it may indicate that in this small percentage the growth has been eradicated before it has gone beyond the line of operation, or it may be an indication of a development of some systemic resistance which we will consider later on.

Another disability is the fact that growths of similar histological appearances and

types may vary considerably in behaviour in different situations and it is useless to try to consider together similar histological groups of cases from more than one situation; this has been done in the case of growths of the mouth, but the result may be quite misleading.

Squamous-cell carcinoma of the region of the mouth may be divided into three types: Growths which show varying degrees of differentiation as shown by keratinization; undifferentiated growths, either transitional-cell carcinoma or lympho-epithelioma.

[Here the speaker showed slides, illustrating transitional-cell carcinoma and lympho-epithelioma.]

Table II, which I showed to this Section some time ago, gives the distribution of

TABLE II.—TYPES OF SQUAMOUS CARCINOMA  
Undiff.

| Site                   | Uncl. | Squam. | Undiff. |         | Total |
|------------------------|-------|--------|---------|---------|-------|
|                        |       |        | Trans.  | L.-epi. |       |
| Tongue, floor of mouth | 12    | 198    | 7       | 2       | 219   |
| Palate .. .. .         | 2     | 24     | 1       | 0       | 27    |
| Cheek .. .. .          | 4     | 28     | 1       | 0       | 33    |
| Lip .. .. .            | 5     | 54     | 0       | 0       | 59    |
| Tonsil .. .. .         | 2     | 23     | 4       | 6       | 35    |
| Pharynx, naso-phar. .. | 11    | 54     | 7       | 7       | 79    |
| Gum, jaw, antrum ..    | 11    | 47     | 11      | 0       | 69    |
| Larynx .. .. .         | 5     | 34     | 5       | 2       | 46    |
| Glands. No primary..   | 2     | 5      | 10      | 7       | 24    |
| Total                  | 54    | 467    | 46      | 24      | 591   |

these growths in various situations. It will be seen that there is a tendency for the undifferentiated types of growth, i.e. transitional-cell carcinoma and lympho-epithelioma to preponderate in certain situations, i.e. tonsil, pharynx, nasopharynx and antrum, and the bad course of such cases is often attributed to the nature of the growth; but further investigation will show that growths in these situations do badly whatever their histological appearance, and Table III A and B shows that

TABLE III.

| Type   | A. % METASTASIS ACCORDING TO TYPE |        |         | Total |
|--------|-----------------------------------|--------|---------|-------|
|        | Uncl.                             | Squam. | Undiff. |       |
| + ve   | 8                                 | 87     | 19      | 114   |
| - ve   | 3                                 | 52     | 1       | 56    |
| Total  | 11                                | 139    | 20      | 170   |
| % + ve |                                   | 63%    | 95%     | 67%   |

| Site   | B. % METASTASIS ACCORDING TO SITE |        |            |                 |        | Total |
|--------|-----------------------------------|--------|------------|-----------------|--------|-------|
|        | Tongue                            | Palate | Cheek, lip | Tonsil, pharynx | Larynx |       |
| + ve   | 55                                | 8      | 12         | 35              | 4      | 114   |
| - ve   | 37                                | 0      | 16         | 0               | 3      | 56    |
| Total  | 92                                | 8      | 28         | 35              | 7      | 170   |
| % + ve | 60%                               | 100%   | 43%        | 100%            | 57%    | 67%   |

growths of the tonsil and pharynx show 100% metastasis although many of these growths were well differentiated histologically. Even the anterior and posterior parts of the tongue are different entities in this respect.

One important defect that I have already stressed is that histological grading is carried out on evidence of rapid growth and of de-differentiation, and rapid growth must not be considered synonymous with malignancy. There are two factors which do not of necessity go hand in hand; one is the rate of growth of the tumour and the other is its invasiveness and liability to secondary deposits. It is true that the two often do coincide, but not necessarily so. Examples of this which have been suggested before are Wilms' tumour of the kidney which may show very rapid

growth but late metastasis, whereas a metastasizing adenoma of the thyroid may show little evidence of rapid growth or de-differentiation. Thus we may have a slowly growing tumour which will invade early but not necessarily show its invasion clinically until the secondary deposits have reached a sufficient size to be obvious. It is this fact that explains the great discrepancy between five and ten year "cures" in carcinoma of the breast, and, as may be expected from the foregoing, this discrepancy may be more marked in cases of lower histological grades, as the more rapidly growing tumours will all tend to kill within the five-year period.

Many successful attempts have been made in the past to correlate histological appearance and behaviour, among which may be quoted the very excellent work done by Cuthbert Dukes (1940) on carcinoma of the rectum, and more recently Thackray and Griffiths have shown that a parallel can be established between histological appearance and behaviour in malignant growth of the kidney; but even bearing these successes in mind there is a considerable amount of work yet to be done in this direction and very many questions still needing answers. For example, why may a tumour maintain a slow rate of growth for long periods? Why may tumours be so relatively constant in their behaviour? This is also true with transmissible tumours in animals, and Professor Gye has provided me with an interesting example of constant behaviour:

"Tumour 113 of the I.C.R.F. carcinoma of the mouse constantly showed granules of glycogen in the cytoplasm through hundreds of transplants. Even when mice hosts were fed on diets which got rid of obvious glycogen from liver, muscle, cartilage, etc., glycogen was still found in the cancer cells and the cells of the bundle of His."

In his classical experiment, McIntosh showed that filtrable tumours could be induced by tar and that such tumours could be transmitted by cell-free filtrates for many passages and continue to be constant in histological type even for as many as 81 passages (McIntosh, 1933; McIntosh and Selbie, 1939). Why is it an uncommon finding for a growth to take on more malignant characters in its secondary deposits, if anything the reverse being the case? Of 110 cases of carcinoma of the breast in which primary and secondary deposits were graded independently only 18 were classified in a lower group and only one in a higher group (Table IV) (Patey and Scarff, 1929).

TABLE IV.—SHOWING NUMBERS OF CASES WITH, AND WITHOUT CHANGES IN MALIGNANCY OF METASTASES

| No. of cases | Metastases in same group | Metastases in lower group | Metastases in higher group |
|--------------|--------------------------|---------------------------|----------------------------|
| 110          | 91                       | 18                        | 1                          |

*Radiosensitivity.*—The increasing use of irradiation therapy and the investigation of the reaction of malignant disease to various rays has necessitated the determination of the factors which make for radiosensitivity or radioresistance. The particular principle, i.e. that radiosensitivity depends to a large extent on anaplasia, seems to be true but so subject to exception that much work needs still to be done in this respect; and it is not complete even if one considers in addition the varying sensitivity of the different normal tissues. For example, some normal tissues may be more radiosensitive than some well-differentiated malignant growths, and here again there is considerable need for evaluation of the various factors concerned.

(3) *Fundamental research into the nature of cancer.*—Here again a morbid anatomist can be of considerable assistance in investigating the undoubted cases of spontaneous retrogression and ætiological factors in the production of cancer, and there is still room for him to work on the natural history of the untreated growth about which very little is known. It is obvious that the natural history of the disease in any

situation is a necessary yardstick before one can assess the effect of any form of therapy. The argument is still continuing as to whether cancer starts in a single cell or in a group of cells.

Another important line that has received too little attention is the investigation of body resistance to carcinoma. Although such resistance is questioned by some it is difficult to explain some of the known facts about cancer without its assumption. This resistance factor can be subdivided into general and local manifestations.

*General.*—It is well known that a carcinoma may be removed apparently completely for long periods up to about twenty years and that at the end of this time recurrences may appear usually in the neighbourhood of the original growth; and although there may be only small recurrences in the site it is interesting to record that most patients showing this late recurrence die very quickly from the disease. This quite unexpected outcome makes one speculate as to what has been happening all the years of latency, and the only possible supposition is that the growth cells have persisted but have been held in check. There are undoubted cases too of spontaneous retrogression of malignant growth, both of the primary growth and of secondary deposits after removal of the primary. It is true these are extremely rare, but, none the less, undoubted examples have been cited from time to time.

*Local.*—Pathologists have said for a long time that certain types of growth show a predilection for the occurrence of secondary deposits in certain situations. For example—carcinoma of the lung shows a high proportion of secondary deposits in the brain and adrenal. There may be an anatomical explanation for some of these but in most cases it is fair to assume that the malignant cells have equal access to many other situations but do not flourish there. It would be better to say that there is a greater resistance in some situations than in others. This is well marked in the case of the spleen, and it may be that, as in infections, a preponderance of the reticulo-endothelium system will inhibit the development of secondary deposits by destruction of the malignant cells.

Another branch of this work is the investigation of the changes produced by the various hormones. This has received some attention, especially in the transplantable fibro-adenomata, and variation in histological appearances can be shown to be the result of treatment by these various hormonal agents.

One further large sphere of activity that is often lost sight of is the fact that all experimental work, whether by transplantation or induction, must be controlled by histological examination.

These are merely examples of some of the ways in which the morbid anatomist can be of assistance in the cancer problem, and no doubt several other investigations will suggest themselves either arising out of these ideas or from personal observation. I hope that it is apparent that morbid anatomy is not yet dead as its detractors would have us believe, and that much that has existed up to now as a hazy impression could be converted into real evidence to be of assistance in cancer research.

#### REFERENCES

- DAWSON, E. K. (1943) *Edinb. med. J.*, 50, 721.  
 DUKES, C. E. (1940) *J. Path. Bact.*, 50, 527.  
 HANDLEY, R. S., and THACKRAY, A. C. (1947) *Brit. J. Cancer*, 1, 15.  
 MCINTOSH, J. (1933) *Brit. J. exp. Path.*, 14, 422.  
 —, and SELBIE, F. R. (1939) *Brit. J. exp. Path.*, 20, 49.  
 MUIR, R. (1941) *J. Path. Bact.*, 52, 155.  
 NEWCOMB, W. D. (1933) *Brit. J. Surg.*, 20, 279.  
 PATEY, D. H., and SCARFF, R. W. (1928) *Lancet* (i), 801.  
 —, — (1929) *Lancet* (ii), 492.  
 SCARFF, R. W., and HANDLEY, R. S. (1938) *Lancet* (ii), 582.  
 TRUSCOTT, B. MCN. (1947) *Brit. J. Cancer*, 1, 129.

## Section of Pædiatrics

President—W. G. WYLLIE, M.D., F.R.C.P.

[September 29, 1948]

### The Present Diagnosis and Therapy of Cystic Fibrosis of the Pancreas

By DOROTHY H. ANDERSEN, M.D.

*Babies Hospital, New York, U.S.A.*

SOME ten years ago I reported a series of 49 cases of cystic fibrosis of the pancreas garnered from the literature and from the autopsy files of the Babies Hospital [1]. Since that time our understanding of the disease has progressed steadily, and contributions to it have been made by many workers in many lands. My present objective is to review the growth in our knowledge and to present the current problems.

The 1938 series of post-mortem cases fell into three groups corresponding to the age at death, with dissimilar clinical stories but essentially identical changes in the pancreas. 5 of the infants of the 1938 series died of congenital small intestinal obstruction, variously diagnosed as meconium ileus, volvulus, obstruction due to a peritoneal band and atresia of the small intestine. The second group was composed of 19 infants who appeared sound at birth, gained poorly in early infancy in spite of normal food intake and died of bronchopneumonia before the sixth month. The third group was composed of 25 children aged 6 months to 14½ years who had gained poorly during infancy, later presented a clinical picture often leading to the diagnosis of coeliac disease, and still later had developed bronchitis, bronchiectasis and sinusitis. Later, when clinical diagnosis was possible and therapy began to have an effect on the life span, the groups were redefined as follows: Group I, patients with congenital intestinal obstruction; Group II, the early group patients with onset of chronic cough before the 6th month; and Group III, the late group of patients with onset of chronic cough after 6 months of age.

The pathological changes are chiefly in the pancreas, lungs and, in Group I, in the intestine. The changes in the pancreas may be interpreted as the result of an abnormality in the secretion, which causes it to be precipitated as eosinophilic material in the lumina of acini and ducts in increasing amounts. Main ducts are often patent but are sometimes plugged with secretion or are atretic. There is a progressive change in age, with increase in the contents of the lumina, and gradual atrophy of acini and replacement by fibrous tissue and sometimes by fat. The islands of Langerhans are unaffected.

The lung changes also vary with the age of the patient. In infants dying of intestinal obstruction in the neonatal period the lungs and bronchi are normal.

In the young infants dying with bronchopneumonia there is an acute purulent bronchitis with *Staphylococcus aureus* as the infecting organism. Bronchogenic abscesses, sometimes perforating to produce pyopneumothorax, may be present and a lobe, or a large portion of one, may become atelectatic because of plugging of a bronchus. In later cases there is diffuse tubular chronic bronchiectasis in the tertiary and smaller bronchi, with thick peribronchial infiltration. The larger bronchi and trachea may be filled with pus in the terminal phase. Cases which have not received dietary and vitamin-A therapy show the squamous metaplasia of the bronchial epithelium resulting from vitamin-A deficiency. In some of the older patients the staphylococcus is accompanied by other organisms, usually of the colon group.

In our own series of congenital intestinal obstruction with fibrocystic disease, now numbering about 14 cases, the infant has usually been surgically explored on the third to sixth day. In the earlier cases of the series the most common surgical diagnosis was volvulus. It is now realized that the cause of the obstruction is the nature of the meconium itself. In the distal portion of the ileum the meconium is hard and grey, resembling dry putty, and cannot pass the ileocecal valve. This material occupies the distal 10-15 cm. of ileum. Proximal to it there is a large loop of ileum distended with dark brown or green sticky meconium and faeces. Because of its size and weight this loop often forms a volvulus or becomes gangrenous because of poor circulation. Farber has shown that the meconium from these infants can be softened by application of pancreatic juice and suggests plausibly that the meconium is abnormal for want of pancreatic digestion [2].

Fatty liver was frequently found in the untreated cases of the early series but has rarely been present in treated cases. Pericholangitis, Laennec's cirrhosis and inspissated secretion in a few bile ducts have occasionally been observed. The gall-bladder is small and contains inspissated secretion but no bile in about one-third of the total number of cases including those of Groups II and III.

Fibrocystic disease frequently occurs in more than one sibling of a family. Twenty family trees have been obtained in an effort to determine the hereditary pattern [3].

Calculations based on Hogben's formula give a mean incidence of 25% of siblings with the disease in affected families. Although this frequency suggests a recessive trait, the pattern of family incidence is against this, since there are more than the expected number of families in which the majority of siblings are affected. A geneticist who was consulted on this point remarked that the pattern suggested either that the concurrence of two factors was required for the expression of the disease, or that the disease was carried as a dominant trait but could be suppressed by a second factor. This irregularity of incidence has practical application in giving advice to parents of two or more children with the disease. The disease may occur in one or both of twins. Sex distribution is about equal. I know of three instances of first cousins having the disease out of about 300 cases of which I have some knowledge. There is suggestive evidence of the occurrence of cases in some of the previous generations. In several instances the majority of siblings of a large family in a previous generation are said to have died of bronchopneumonia in early infancy, and in one family with two infants with meconium ileus there was a maternal aunt who died of intestinal obstruction in the neonatal period. It seems probable that in another decade or so there will be evidence as to the transmission of the disease to offspring of known cases.

The diagnosis of the disease may be suspected from the clinical picture but must be confirmed by laboratory means. Since early diagnosis greatly improves the prognosis we frequently consider the possibility of this disease in differential diagnosis of infants with malnutrition.

The clinical picture on hospital admission is quite variable. In Group I the meconium ileus may be recognized at operation by a surgeon who is familiar with it. However, the obstruction is often attributed to the volvulus or to congenital bands found about the ileum, and the inspissated meconium is therefore left and continues to block the lumen.

One of the surgeons of the Babies Hospital, Dr. Robert Hiatt, has devised a procedure which has been successful in 5 of 8 cases [4]. This consists of making an incision at the junction of the dilated loop of ileum and the distal portion containing the inspissated meconium. After clamping the proximal loop the distal loop is dilated with saline to separate the firm and moulded meconium from the mucosa, after which the meconium is milked out. The procedure is repeated until the saline passes freely into the colon. The distal loop is then clamped and the procedure repeated on the proximal loop. The incision is then closed. In one case it was necessary to remove the loop forming the volvulus. A diluted solution of pancreatin is given by gastric tube. When feedings are begun they consist of protein milk, glucose and casein hydrolysate.

The cases of Group II with early onset form the majority of all cases of fibrocystic disease. The most characteristic picture is that of an infant aged 2-6 months who appeared normal at birth but is slow in regaining his birth-weight and continues to gain slowly in spite of an excellent appetite and adequate feeding. After some weeks of poor gain he develops a respiratory infection and is admitted with a diagnosis of bronchopneumonia. Sometimes he is admitted as a feeding problem and the respiratory infection appears later. The stools may appear normal except for a slight increase in number. There are also some patients of this group who have diarrhoea in the early months. Differential diagnosis in this age-period includes poor feeding, early coeliac disease, pertussis, lipoid pneumonia, epidemic diarrhoea of the newborn, asthma, early megacolon, and atelectasis due to foreign body aspiration.

The cases of Group III, with onset after six months, may give a history of having had mild diarrhoea in the neonatal period but rarely have had watery stools after the sixth month. Stools are increased in bulk and often in number and after the first few months are foul with a distinctive odour which one mother described as resembling stale marigolds. The experienced nurse can often make the diagnosis by olfactory sense alone. There may have been a cold or bronchitis in the early months which responded to penicillin. In some cases the physical contours and foul stools have led to the diagnosis of coeliac disease in the second year. Colds are frequent and prolonged but the cough may not be constantly present for some years. Sooner or later the respiratory symptoms dominate the picture and the child has a barrel chest, cyanosis, clubbed fingers, and a paroxysmal cough. In the differential diagnosis of this group the conditions to be considered include coeliac disease, asthma, chronic bronchiectasis, and tuberculosis.

So far the most reliable laboratory means of confirming the diagnosis is the assay of duodenal juice for pancreatic enzymes [5]. Preliminary observations on a series of normal infants and children have shown that trypsin and lipase are present from birth, whereas amylase is not found for the first two or three months of life, and there is normally a wide variation in its concentration during the age-period of 3-6 months. Amylase is usually low or absent in older infants and children with coeliac disease. The absence of amylase cannot therefore be used as a means of diagnosis of fibrocystic disease. In our studies the viscosimetric method was used for the assay of trypsin and amylase and the Willstädter method for lipase. Although both lipase and trypsin are present throughout infancy, in our hands the method for the determination of trypsin is more sensitive and gives better checks than that for lipase, and we have therefore used the trypsin concentration of the duodenal juice as the



means of determining pancreatic deficiency. In extreme marasmus from any cause and in dehydration the trypsin concentration may be reduced and the findings equivocal, and the test must be repeated after the clinical condition of the infant has improved. In the great majority of cases of fibrocystic disease the trypsin concentration is under 10 viscosimetric units per c.c. while the highest figure obtained has been 40 units. Normal infants usually have a trypsin concentration of over 200 units per c.c., while in marasmic infants the figure often lies between 40 and 100 units.

The viscosimetric determination of the trypsin is a laborious procedure. Because of our policy of suspecting the presence of fibrocystic disease in an attempt to pick up early cases, we have found it advisable to apply a screening test in order to reduce the number of enzyme determinations to the capacity of the laboratory. Two such screening tests have been used. The first is the microscopic examination of faeces for fat [6]. All infants with fibrocystic disease have steatorrhœa when fed whole milk without pancreatin. When microscopic examination of faeces obtained under these conditions demonstrates no fat droplets the diagnosis may be discarded. We have begun to use a second screening test, developed by Shwachman in Boston Children's Hospital which appears to be satisfactory in the younger age-group [7]. This is the use of X-ray film, with the gelatin scraped from one side. The film is cut to the size of a Petri dish and placed gelatin side up. Pancreatin is withheld from the patient for two days before the faeces are obtained. About 1 gramme of faeces is diluted with water at 1 : 5 and 1 : 10 and a drop of each dilution placed on the film with a control drop of water. The dish is covered and left in an incubator at 37° for one hour. In most normal infants the test will show digestion of the gelatin but in cases of fibrocystic disease and in a few older normal children there will be no digestion. It has been found that a solution containing approximately 0.2 viscosimetric units of trypsin will give a positive test.

Other features of the disease have been explored for their value as diagnostic procedures. The vitamin-A absorption curves are affected by steatorrhœa from whatever cause and a flat curve is not specific for pancreatic deficiency. The chemical analysis of faeces for nitrogen is reliable but tedious, while analysis for fat is reliable only when an excess of neutral fat is recovered. An amino-acid absorption curve based on the determination of serum amino acids after ingestion of casein or gelatin is said to be a reliable means of diagnosis but also requires special techniques [8].

#### TREATMENT

There are two main methods of treatment: dietary therapy which attempts to compensate for the defective digestion and chemotherapy directed at the respiratory infection [9, 10].

The plan of dietary therapy is based on accumulated information in the literature of physiology with regard to the effect of pancreatectomy in animals and on a number of balance studies on patients with fibrocystic disease. It has been found that on a mixed normal diet these patients will excrete about half of the fed protein, half the fed fat, and about 15% of the fed carbohydrate [11, 12]. In most studies the nitrogen retained from the food is barely adequate to meet the estimated needs, and it appears probable that this is the factor limiting growth in these children. Theoretically it would seem rational to provide nitrogen as amino acids, but most children of spirit will resist ingestion of the amount of amino acids necessary to supply their total protein requirements. Small amounts may be successfully administered. A positive balance and good growth have been obtained on a daily intake of 6-8 grammes of protein per kilogram of body-weight, of which casein hydrolysate forms 1-1.5 grammes.

Fat is poorly absorbed and also poorly tolerated. As a source of calories carbohydrate can be substituted. A limited amount of fat should be given, with

care to provide ample amounts of all known and probable fat-soluble essential substances. For this reason the diet should include one or two eggs a day, and a fish-liver oil. Skimmed milk is given and fried foods are forbidden. We have evidence that some fat is absorbed, and that a low dietary fat leads to a larger proportion of fat being absorbed. Vitamin A is fairly well absorbed when a low fat diet with pancreatin is given, and we have assumed that the same may be true of other fat-soluble essential substances.

Sugars and polysaccharides do not require pancreatic digestion, and balance studies suggest that some starch may be utilized without the action of pancreatic juice. The carbohydrate intake should therefore be high, since it is the chief source of calories. It is provided as fruits, vegetables, sugars and moderate amounts of cereal foods.

Because of hunger and their digestive handicap, we give frequent feedings to the infants and encourage between-meal snacks in older children.

Supplements include a fish-liver oil concentrate sufficient to provide 30,000 units of vitamin A daily. Vitamin-B complex is given orally and is especially necessary in the younger infants with diarrhoea. Pancreatin is provided at levels of 1-2 grammes per meal. It is of definite benefit in marasmic infants and has some effect, as judged by balance studies, in older children who are doing well.

In practice it is the young infants who respond most dramatically to dietary therapy alone. The special digestive difficulty of these infants is shown by failure to regain the birth-weight for several weeks and by their failure to gain normally on less than 150-200 calories per Kg. Hypoproteinæmia and evidence of vitamins A and K deficiency are also encountered more frequently in the younger age-group. Three years ago a formula now known as Mead-Johnson No. 235 was devised by us for infants who had survived operation for meconium ileus [4, 13]. The mixture is composed of protein milk 50%, casein hydrolysate 5%, banana powder 25%, glucose 20%. It is based on the observation that the use of a formula composed chiefly of amino acids and glucose led to a high post-prandial rise of these substances in the blood followed by a prompt fall in blood levels and loss in the urine. Feeding with protein milk and cereal led to a large faecal loss. It seemed reasonable that a judicious mixture of these substances would solve the problem, and this has in fact worked very well.

It has also seemed advisable to commence feeding solids in the form of puréed fruits, bananas and meats at an early age, about 3 months, as a means of providing necessary minerals and calories. Cereal has been withheld until about 1 year of age.

Skim milk with added sugar is substituted for Number 235 in the latter half of the first year. By the third year the diet approaches a normal one with several notable exceptions. Skim milk and double portions of protein foods and an abundance of sugar and fruit are given, cereal foods are limited to one serving per meal, and all foods of high fat content such as cream, ice cream and fried foods are prohibited. For the sake of morale, ice cream is allowed once a week.

#### RESULTS

Several weight curves and photographs of patients were then shown as examples of the success of this regime. These included a group of patients successfully treated for meconium ileus, the oldest now 3 years of age; and several children in whom diagnosis was made early because of the presence of the disease in a sibling.

The success of therapy of the respiratory infection associated with fibrocystic disease is dependent on two factors: (1) the phase of the infection at which therapy is instituted, and (2) the sensitivity of the infective bacteria to the chemotherapeutic agents available. Experience has shown that if the cough has been present for only a few weeks and the infecting agent is a staphylococcus sensitive to penicillin,

the infection may be so well controlled that all clinical and roentgen signs of it disappear. A mild infection with an organism which is insensitive to available agents frequently progresses to a fatal termination in a few weeks or months. A chronic bronchitis, with roentgen findings of thickened bronchovascular markings and even with diffuse "snow-flake" lesions through the lung parenchyma but with a sensitive organism, may give a dramatic clinical response to therapy.

Damage to the bronchi, especially diffuse tubular bronchiectasis, may remain, with persistent thickening of bronchial shadows as seen by X-ray. Patients who have responded to chemotherapy but retain damage to the bronchi have increased in number since penicillin was first available to us four years ago and have presented new problems of management. In spite of good nutrition and activity these children have a cough, usually on rising, and a tendency to recurrent infection. Those with most severe changes sometimes develop bronchitis due to *Ps. pyocyaneus* or other Gram-negative bacilli, a complication rarely seen before the days of penicillin. Though this infection may respond to streptomycin the prognosis is poor, since this type of infection is associated with severe and irreversible anatomical damage. Several of these children have survived their pulmonary infection only to die in right heart failure, another clinical picture not seen before penicillin was available.

We have developed certain policies in regard to the use of the newer drugs on a more or less empirical basis. These policies have altered and are still changing with experience. The following is a statement of our present routine rather than a perfect plan of therapy. The actual procedure is as follows: When a child is admitted to the hospital with the clinical picture and tentative diagnosis of fibrocystic disease, the preliminary work-up is brief and both dietary and penicillin therapy are started on the day of admission. The work-up considered necessary prior to beginning therapy consists of obtaining cultures of the nose and throat, and if possible of sputum, and an X-ray of chest. The cultures are sent to the laboratory for sensitivity tests to penicillin and other drugs but therapy is not delayed for these reports. Other data to be obtained before the end of the second day in hospital are (1) serum protein, (2) serum vitamin A and carotene, (3) blood-count, (4) urine examination, (5) microscopic examination of faeces for fat. After clinical improvement the diagnosis is confirmed by assay of the duodenal juice for trypsin.

Because the usual infecting organism is a staphylococcus which is sensitive to penicillin, this drug is used first. Large doses are used, since experience has shown that the effective doses are similar to those required for subacute bacterial endocarditis, and since staphylococci tend to develop resistance to penicillin. Oral penicillin or penicillin in wax given only twice a day are forbidden these patients. At present for the first course, the usual dose is 100,000 units by intramuscular injection and the same by aerosol every three hours for seven to fourteen days.

Penicillin by inhalation is a valuable therapeutic weapon in these cases and is much more effective here than in the chronic bronchiectasis of adults where the flora is usually varied. It is considered as a topical application of penicillin, with the purpose of applying the maximum amount of the drug to the site where, as shown at post-mortem examinations, the greatest concentration of bacteria exists. Most children of 18 months or over can be taught to co-operate in the administration of aerosol by mask, but the younger patients and the extremely ill are given aerosol into an oxygen tent. The frequency of the treatments is increased in these patients to 100,000 units hourly.

Because of the tendency of the staphylococcus to develop resistance to penicillin we have been avidly grasping new drugs as they become available. So far we have used in the same manner the following antibacterial drugs: Streptomycin, Bacitracin, Sulphathiazole, Polymyxin B and Aureomycin. Our experience with some of these

is limited and I can make only a few useful statements about them. Streptomycin is highly effective against Gram-negative organisms and can be used by aerosol in surprisingly large doses, partly because it diffuses poorly and partly because it is largely coughed up with the sputum. Bacitracin is so far the only agent effective in cases with penicillin resistance but it has two drawbacks, probably due to impurities. Some batches are highly irritating to the nasal mucous membranes and some batches produce oliguria and an elevated serum non-protein nitrogen. Other batches are without these defects and it is probable that this agent will be of greater usefulness before long.

The following cases illustrate some of these points. Both were of the older group, Group III, and had chronic lung changes when first seen. Marguerite was one of the first patients to receive penicillin aerosol, in July 1944. At that time we were able to obtain only enough for a dose of 5,000 units every three hours for five days. This was administered by aerosol through a catheter to the posterior nasopharynx, since we had not as yet devised the mask technique.

On admission Marguerite was 4 years old, had had intermittent cyanosis for four months, continuous cyanosis for several days and was extremely ill. Her response was dramatic but she relapsed after a week or so, and received several courses of penicillin at low dosage—all that we were able to obtain, however. I now consider it mere good luck that she did not develop resistance to the drug. After three courses of aerosol over a period of two months, she continued to improve without it, with disappearance of clubbing and reduction of chest circumference by 2 in. She continued to do well until June 1948, when an attack of influenza was followed by a productive cough and loss of weight. She received another course of penicillin in July and is again doing well at the age of 8 years.

Sidney presents a more gloomy picture. On admission he was not as ill as Marguerite had been, but cultures from his throat and sputum grew a staphylococcus with high resistance to penicillin. His chart illustrates the usual course of these patients and also the rather fumbling manner in which we are still using the newer drugs.

It is apparent that chemotherapy applied early in the course of infection with a sensitive organism may result in control of the infection; the prognosis of patients who have once had a severe chronic infection is still uncertain.

In spite of the advance in our knowledge there remain many unsolved problems. The most pressing of these is the relationship between the respiratory infection and the pancreatic deficiency. There are at present two hypotheses as to the ætiology of the respiratory infection. The older of these is the theory that the infection follows deficiency of some nutritional substance required for the normal function of the bronchi, a deficiency resulting from the lack of pancreatic secretion. The other hypothesis is that the bronchial secretion is congenitally abnormal in a manner analogous to the pancreatic secretion. This question has not been definitely settled. The arguments for the congenital theory are based on the constancy with which the infection appears, the acknowledged occasional occurrence of abnormalities of glands other than the pancreas in these cases, and the viscosity of the exudate in the bronchi. The nutritional theory, which I hold, is based on the knowledge that untreated patients with fibrocystic disease are sometimes deficient in certain nutritional factors, such as vitamin A, and that most patients in whom early diagnosis has led to early appropriate dietary therapy have not developed a chronic respiratory infection [13]. Much more investigation is required before we can accurately assess the defects in nutrition of these children, especially with respect to fat-soluble essential substances. The basic question will not be solved until we have evidence that these children are deficient in a specific substance known to be required by the bronchi, or until, on the other hand, a specific abnormality of the bronchial mucus is demonstrated to be congenital.

The evidence for the intestinal theory is sufficiently strong so that the patients should be given dietary therapy based on our present understanding of their needs.

A case is presented of a child of  $7\frac{1}{2}$  years who was diagnosed and started on dietary therapy at the age of 6 weeks. She has continued free of respiratory infection, has maintained a normal growth curve, and leads an active and normal life, except for moderate dietary restriction.

#### SUMMARY

Our knowledge of cystic fibrosis of the pancreas has progressed to a point where a clinical diagnosis can be made early in the disease. Response to a combination of dietary therapy and chemotherapy depends on the sensitivity of the infecting bacteria to available chemotherapeutic agents and on the stage of the pulmonary lesion when therapy is begun. Early diagnosis and therapy lead to an improved prognosis, and may result in freedom from respiratory infection, at least for the span of years over which observation has been possible. The urgent unsolved problem is the discovery of the cause of the respiratory infection. There is strong presumptive evidence that it is due to a specific nutritional deficiency.

#### REFERENCES

- 1 ANDERSEN, D. H. (1938) *Amer. J. Dis. Child.*, 56, 344.
- 2 FARBER, S. (1944) *J. Pediat.*, 24, 387.
- 3 ANDERSEN, D. H., and HODGES, R. G. (1946) *Amer. J. Dis. Child.*, 72, 62.
- 4 HIATT, R. B., and WILSON, P. E. (1948) *Surg. Gynec. Obstet.*, 87, 317.
- 5 ANDERSEN, D. H. (1942) *Amer. J. Dis. Child.*, 63, 643.
- 6 — (1945) *Amer. J. Dis. Child.*, 69, 141.
- 7 SHWACHMAN, H. (1947) (Personal communication).
- 8 WEST, C. D., WILSON, J. L., and EYLES, R. (1946) *Amer. J. Dis. Child.*, 72, 251.
- 9 ANDERSEN, D. H. (1945) *Amer. J. Dis. Child.*, 70, 100.
- 10 DI SANT'AGNESE, P. E. A., and ANDERSEN, D. H. (1946) *Amer. J. Dis. Child.*, 72, 17.
- 11 SHOHL, A. T., MAY, C. D., and SHWACHMAN, H. (1943) *J. Pediat.*, 23, 267.
- 12 ANDERSEN, D. H. (1945) *Amer. J. Dis. Child.*, 69, 221.
- 13 — *Pediatrics* (in press).

## Section of Odontology

President—Professor SHELDON FRIEL, M.Dent.Sc., Sc.D., F.D.S.

[October 25, 1948]

### Orthodontic Diagnosis

#### PRESIDENT'S ADDRESS

By Professor SHELDON FRIEL, M.Dent.Sc., Sc.D., F.D.S.

AN orthodontic diagnosis must be reached by a comparison of the maldevelopment and malfunction with normal development and function of the face and jaws of a child of the same developmental period. A comparison of the malocclusion of the teeth with ideal occlusion is merely a diagnostic aid. In addition, for a full diagnosis, the ætiology of the condition must be known.

Many conditions in medicine are not fully diagnosed because the ætiology is unknown and certainly in orthodontics comparatively few cases of major malformation of the face and jaws can be fully diagnosed. The reason for this is that the original cause may have occurred quite early in life and it, in turn, has brought in other factors, so it is almost impossible to obtain a sufficient history when the patient is first seen at the age of 9 or 10 years. One can make only a tentative suggestion as to the cause of the malformation.

There are some orthodontists who hold the view that the diagnosis of malocclusion must be based on a comparison with the average development and occlusion of a child of the same age or developmental period. I cannot agree with this. Statistical analyses of development are most valuable in showing the direction of growth. Anatomical markings on the head are known on the average to show certain relationships but the deviations from the average are too great to enable one to apply them to the individual. Hellman [1] devised a scheme whereby the occlusion of the teeth was divided up into a series of contacts, such as cusp and fossa contact. Altogether he found that there were a possible 138 contacts in an ideal adult occlusion, but that the average for a large number of almost perfect occlusions was 124 contacts with a standard deviation of 8. The fallacy of such a method of diagnosis of the occlusion of the teeth can be seen in one of my cases which had the upper incisors protruding, a loss of 13 contacts, but with all other contacts correct. It has more than the average number of contacts but functionally and æsthetically is grossly abnormal; while a case that had every contact a little wrong would be classed as a gross malocclusion though functionally and æsthetically it was almost normal.

Other methods of diagnosis have been used extensively. Most of these methods have been based on one anatomical characteristic around which the diagnosis has been built. Take [2] for example, the relation of the lower first permanent molar to the upper first permanent molar. Now it has hitherto been assumed that the upper molar was always in a definite position in relation to the skull. It is now known that in only a proportion of cases is the upper molar in this definite position. Again there is the standard of measurement known as Simon's Orbital Plane [3], which was supposed to pass through the point of the cusp of the upper canine in normal cases. Abnormal cases were diagnosed by the deviation from this plane. In point of fact, however, this plane has been found to vary [4] a great deal where it crosses the canine at different stages of growth.

More recently [5, 6] the inclination of the lower incisors to the lower border of the mandible has been used as a criterion. This one characteristic is quite insufficient as the basis for diagnosis and in my opinion this method will suffer the same fate as the other two. Each is correct in only a proportion of cases and in *only* a proportion. In reality, each is not a method of diagnosing the cause of the condition, since it ignores causation, but is a basis for treatment. Each assumes that a deviation from the average or mean of the general population is abnormal for the particular case under review and therefore offers the hypnotic suggestion to the perplexed clinician that the restoration of that case to within a certain measured distance from the mean or average will lead to a good functional, æsthetic and stable result. Some people also decline to delve more than a certain distance into the ætiology of the condition on the grounds that further differentiation would not, at present, influence their treatment. To my mind this process of reasoning is quite wrong because: (1) If the ætiology were more fully known, better treatments would be devised; (2) the explanation of the good response to treatment in some cases and the failure in others lies, to a great extent, in hitherto unexplained ætiological factors; and (3) I believe that in the field of preventive orthodontics we shall only be able to prevent maldevelopment when we have a sound knowledge of the causes, inherited, prenatal or postnatal, which produce the defect.

Orthodontic diagnosis cannot be an exact science and to a great extent it must be the result of individual knowledge and experience. The variation in the shape of the head and of the relationship of the teeth to points or lines is so great in the individual and at different periods of growth that judgment must be formed as to whether the case is abnormal or normal for that individual. I do not want to give the impression that statistical methods are of no value. They are an essential part of every investigation but what I do wish to emphasize is that in their application to the individual they should not be slavishly followed. We all use these single characteristics to assist in the analysis of a case. The modern tendency is for medical and dental sciences to rely too much on instruments for measurement and too little on clinical observation. It is comparatively easy to teach undergraduates and post-graduates to use measuring instruments in diagnosis but it is exceedingly difficult to teach clinical observation.

Most orthodontic diagnoses are made from teeth only, their relationship to each other in their own arch and the relationship of the arches to one another. I think this is a wrong approach. The first thing that I do is to observe the way the child walks into the room, the general posture, the build of the child, the relationship of the lips at rest and if possible the way the lips and jaws move during talking. The next step is a more detailed observation of the relationship of the jaws to one another and to the rest of the face in an antero-posterior, lateral and vertical direction. Only then do I look into the mouth. The arch relationship should conform to the previous observations of the jaw relationship though it can be obscured by individual movements and inclinations of teeth and arrest of growth due to local factors such as premature extraction of teeth. It can also be obscured by the amount of development of the chin or face. There are varieties of normal chins from the protruding shelf below the apices of the teeth to the almost vertical chin that is nearly in the same place as the alveolar bone. It must be remembered, too, that the lower jaws can be normal and that the malrelation may be due entirely to the upper face. The form of the arches and their relationships to the basal bone, the individual malpositions and inclinations of teeth and how they came to take up their positions have to be recorded. After this I look for any special points which may have arisen during the examination, such as tonsils, swallowing, nasal insufficiency, habits, &c. The history of the case should follow in order to see if it is possible to discover the aetiology and whether the cause is still in operation. It does not require a complicated chart to record these observations but it does mean that a systematic examination has been carried out.

Photographs of patients are of limited value. They, like models, are of the patient at one particular moment but do not give a clear picture of the individual in all his or her movements, colouring, tone or posture. Much more information can be obtained in observing the child in all his or her movements and posture.

It is evident that a good diagnostician must have a very considerable knowledge of the manner of growth of the jaws, of the changes in occlusion of the teeth during growth and of the normal function of the parts; he must be observant to detect any departure from the normal and he must have sufficient experience to know if it is abnormal for that individual.

A great deal of information has been obtained during the past twenty-five years as to the manner of growth of the jaws from the experimental work of Brash [7, 8, 9], Charles [10] and Rushton [11], and from Broadbent's cephalometric radiographs of the same individual over a long period of years. Broadbent [12, 13, 14, 15] has shown that there is an alteration in the direction of growth during the first three years of life but after that the normal direction of growth continues along more or less parallel lines. It is upon the basis of normal growth as demonstrated by work of this kind that the orthodontist forms his diagnosis of the abnormal. For instance [16] he is enabled to understand the direction of the migrations of the teeth following the extraction of deciduous or permanent teeth; and that, following an extraction, there is an inhibition of the normal forward growth anterior to the site of the extraction, which could be mistaken for a posterior drift of the teeth.

There are four groups of factors that may affect the form of the jaws and consequent alignment and relationship of the teeth. The first group, and probably the most important, is the inherited pattern for the size and form of the jaws. It can be modified to a certain degree by treatment but more important still it can be altered for better or worse, mainly the latter, by one or all of the three other groups of factors. These three groups are function, systemic disease and local factors. The differentiation of these four groups is the crucial part of diagnosis.

The inherited size and form of the lower jaw can be considerably increased and altered by the imposition of a local factor. For example, the upper incisors can be locked inside the lower incisors due to extensive extraction of the deciduous teeth before the age of 5 years and can produce a true prenatal lower jaw. On the other hand it is doubtful if an inherited large lower jaw can be prevented, to any appreciable extent by the methods at our disposal, from attaining its predetermined full size.

The effect of muscle pressure on the growth of the jaws and alignment of the teeth has been emphasized in numerous textbooks and papers. Salzmann [17], in describing the "Division of occlusal force", says: "The anterior resultant force aids in the forward and lateral growth of the dentures and helps to maintain the proximal contact of the teeth. The orbicularis oris and its associated muscles in conjunction with the buccinator prevent the denture from being carried too far forward. The denture reaches an apparently fixed form and position when all the forces acting upon it are in a state of balance. This balance may be disturbed at any time resulting in a noticeable tooth movement or shifting which continues until balance is restored." Turner [18] in his Tomes Lecture delivered at the Royal College of Surgeons, July 1947, describes a case, aged 9-10 years, suffering from adenoids, in which one upper first permanent molar had been extracted previously, the second molar being in contact with the second premolar. He claims that the incisors, canines and premolars on the side of the extracted tooth had been driven backwards and inwards by lip and cheek pressure. Hemley [19] states: "The lips (orbicularis oris) and cheeks combine to act as a powerful force on the dentition, the former pressing on the labial and the latter on the buccal surfaces of the teeth." Brodie [20] writes: "There is a condition of antagonism between the tongue on the inside and the lips and cheeks on the outside and this antagonism largely determines the inclination and position of the teeth and alveolar processes in all cases except in those where maleruption, slow growth, or occlusal interference can be shown. Even in these cases it plays a powerful rôle. Given sufficient development of the alveolar process to accommodate the teeth, the tongue, lips and cheeks will determine arch width and apical inclination and whether we like the result or not cannot make them otherwise and maintain them." I wonder if too much stress is not being laid on the part played by muscles? The effect of muscular development affects growth and development by: (1) The strength of the muscles. (2) Muscle tone. (3) The rest position of the muscles and the anatomical parts they control.

I do not think there is any evidence that increased strength of the masticatory group of muscles directly makes the jaws grow larger, though indirectly they may bring greater blood supply. They can cause an increase in the density of the bone to withstand the pressure and an increase in their area of attachment. Indirectly by causing wear [16] of the deciduous crowns they release the lock which allows the normal changes in relation of lower and upper deciduous arches to take place between 3 and 6 years of age.

The majority of people do most of their chewing on one side of their mouth, the more frequent side being the left. Muscles tests have also shown that, on the average, the force that can be exerted on a dynamometer is greater on the left than the right side. It is possible that this selective form of chewing does account for the very frequent exaggeration of the malocclusion on one side, especially of the type of non-forward movement of the lower deciduous arch between 3 and 6 years of age.

The muscles of the lips and cheeks have no more pressure on the teeth than the extensor muscles of the fingers have on the head of the metacarpal bone. The bones of the pelvis are not completely flattened out no matter how long we sit. The buccinator produces no pressure at all on the cheek teeth except indirectly keeping food between teeth during mastication. Its area of attachment is on an outer plane to the buccal surfaces of the teeth. One sees cases where the lips are not used and the upper incisors are visible almost the whole time and yet the incisors do not protrude. It must be remembered that where pressure is applied to the surface of a bone by the contraction of muscles, there is a cushion of fat or a form of lubrication which distributes the pressure and I think the same applies to the tongue, lips and cheeks.

The tongue does not occupy the whole of the oral cavity no matter how strong it is. There is a considerable area at the back of the tongue that is not in contact with the palate and also the area beneath the tongue in the anterior region.

Muscle tone and posture are closely interrelated. I do not think there is any doubt that abnormal posture and function of muscle groups can greatly influence the alignment of the teeth. In normal posture the teeth are kept nearly in occlusion, the lips together and the anterior portion of the tongue lying in contact with the anterior part of the palate and cingula of the upper incisors. Abnormal posture can produce malocclusion of the teeth. For example—in a habitual mouth-breather associated with a post-normal relationship of the lower jaw to the upper jaw, the tongue lies in the floor of the mouth, the lips are apart and the lower lip, due to the post-normality of the lower jaw, can get behind the upper incisors and make them incline labially. Large arches can result from the pressure of an abnormally large tongue.

Rix [21] has made a very important contribution to our knowledge of the ætiology of malocclusion by drawing attention to the normal methods of swallowing. The normal individual whose teeth have erupted closes his teeth together and presses his tongue against the anterior portion of his palate and against the cheek teeth when swallowing. In infants, on the other hand, the tongue lies between the gum pads and the cheeks act as the resistance.



Orthodontic diagnosis cannot be an exact science and to a great extent it must be the result of individual knowledge and experience. The variation in the shape of the head and of the relationship of the teeth to points or lines is so great in the individual and at different periods of growth that judgment must be formed as to whether the case is abnormal or normal for that individual. I do not want to give the impression that statistical methods are of no value. They are an essential part of every investigation but what I do wish to emphasize is that in their application to the individual they should not be slavishly followed. We all use these single characteristics to assist in the analysis of a case. The modern tendency is for medical and dental sciences to rely too much on instruments for measurement and too little on clinical observation. It is comparatively easy to teach undergraduates and post-graduates to use measuring instruments in diagnosis but it is exceedingly difficult to teach clinical observation.

Most orthodontic diagnoses are made from teeth only, their relationship to each other in their own arch and the relationship of the arches to one another. I think this is a wrong approach. The first thing that I do is to observe the way the child walks into the room, the general posture, the build of the child, the relationship of the lips at rest and if possible the way the lips and jaws move during talking. The next step is a more detailed observation of the relationship of the jaws to one another and to the rest of the face in an antero-posterior, lateral and vertical direction. Only then do I look into the mouth. The arch relationship should conform to the previous observations of the jaw relationship though it can be obscured by individual movements and inclinations of teeth and arrest of growth due to local factors such as premature extraction of teeth. It can also be obscured by the amount of development of the chin or face. There are varieties of normal chins from the protruding shelf below the apices of the teeth to the almost vertical chin that is nearly in the same place as the alveolar bone. It must be remembered, too, that the lower jaws can be normal and that the malrelation may be due entirely to the upper face. The form of the arches and their relationships to the basal bone, the individual malpositions and inclinations of teeth and how they came to take up their positions have to be recorded. After this I look for any special points which may have arisen during the examination, such as tonsils, swallowing, nasal insufficiency, habits, &c. The history of the case should follow in order to see if it is possible to discover the aetiology and whether the cause is still in operation. It does not require a complicated chart to record these observations but it does mean that a systematic examination has been carried out.

Photographs of patients are of limited value. They, like models, are of the patient at one particular moment but do not give a clear picture of the individual in all his or her movements, colouring, tone or posture. Much more information can be obtained in observing the child in all his or her movements and posture.

It is evident that a good diagnostician must have a very considerable knowledge of the manner of growth of the jaws, of the changes in occlusion of the teeth during growth and of the normal function of the parts; he must be observant to detect any departure from the normal and he must have sufficient experience to know if it is abnormal for that individual.

A great deal of information has been obtained during the past twenty-five years as to the manner of growth of the jaws from the experimental work of Brash [7, 8, 9], Charles [10] and Rushton [11], and from Broadbent's cephalometric radiographs of the same individual over a long period of years. Broadbent [12, 13, 14, 15] has shown that there is an alteration in the direction of growth during the first three years of life but after that the normal direction of growth continues along more or less parallel lines. It is upon the basis of normal growth as demonstrated by work of this kind that the orthodontist forms his diagnosis of the abnormal. For instance [16] he is enabled to understand the direction of the migrations of the teeth following the extraction of deciduous or permanent teeth; and that, following an extraction, there is an inhibition of the normal forward growth anterior to the site of the extraction, which could be mistaken for a posterior drift of the teeth.

There are four groups of factors that may affect the form of the jaws and consequent alignment and relationship of the teeth. The first group, and probably the most important, is the inherited pattern for the size and form of the jaws. It can be modified to a certain degree by treatment but more important still it can be altered for better or worse, mainly the latter, by one or all of the three other groups of factors. These three groups are function, systemic disease and local factors. The differentiation of these four groups is the crucial part of diagnosis.

The inherited size and form of the lower jaw can be considerably increased and altered by the imposition of a local factor. For example, the upper incisors can be locked inside the lower incisors due to extensive extraction of the deciduous teeth before the age of 5 years and can produce a true prenatal lower jaw. On the other hand it is doubtful if an inherited large lower jaw can be prevented, to any appreciable extent by the methods at our disposal, from attaining its predetermined full size.

## Section of Urology

President—TERENCE MILLIN, M.A., M.Ch., F.R.C.S.

[October 28, 1948]

### The Ureter, the Gynæcologist and the Urologist<sup>1</sup>

#### PRESIDENT'S ADDRESS

By TERENCE MILLIN, M.A., M.Ch., F.R.C.S.

THERE are many problems in connexion with the surgery of the ureter in which team-work between the two specialties of urology and gynæcology is essential (and team-work is the key to good medicine to-day).

This paper is an attempt to bring to the notice of both urologists and gynæcologists some facts perhaps too little appreciated, some problems still awaiting solution, and to illustrate, when possible with case reports, procedures which we have adopted with varying degrees of success. *Our two specialties cannot remain watertight compartments when it is the patient we are endeavouring to make watertight.*

I propose to consider the following aspects of ureteric surgery:

- (a) Congenital abnormalities of the ureter important to the gynæcologist.
- (b) The ureter injured in gynæcological interventions.
- (c) The ureter in pregnancy.
- (d) The ureter in inflammations and benign tumour of the pelvis.
- (e) The ureter in genital prolapse.
- (f) The ureter in carcinoma of the cervix.
- (g) The ureter in anuria.

In considering some aspects of the normal anatomy and physiology of the ureter I shall deal briefly with two points: First, the distribution of the blood-vessels in relationship to the lower end of the ureter, for I find that most postgraduates are singularly untutored in this important piece of applied anatomy (fig. 1).



FIG. 1.—Operative exposure of lower end of ureter showing distribution of main vessels.  
(After Fey.)

I believe that more of the bad results of uretero-colic anastomosis are due to unduly tight suturing than to reflux. We now employ only a very short submucosal trough

Secondly, the other anatomical aspect of the normal ureter which I wish to mention is the postero-lateral pelvic curve. By mobilizing the ureter and straightening out this curve it is possible to shorten its course by several centimetres. Knowledge of this will often be useful when effecting a uretero-vesical anastomosis.

Turning to the applied physiology of the ureter, the well-known intrinsic neuromuscular mechanism and ample anastomosing blood supply allows for free surgical liberation without detriment. In my view, one of the most important aspects of ureteric physiology to the operating surgeon is the lowness of the intra-ureteric pressure, and the disastrous results in the shape of upper tract dilatation, stasis, infection and finally renal incompetence if surgical interference leads to compression of the tube. I know of three deaths from anuria proved at autopsy to have been due to extrinsic pressure on both ureters from a retroperitoneal hæmatoma following hysterectomy, presumably due to a slipped ligature. I shall deal later with the diagnosis and treatment of this type of case. For all surgery either directly on, or in the neighbourhood of the ureters the low intra-ureteric pressure must be kept constantly in mind.

<sup>1</sup>The paper was illustrated by slides.

Rix has shown that the infant type of swallowing may persist to the detriment of the occlusion of the teeth.

The following case may be of interest: A girl, aged 18 years, was sent to me on account of the wearing down of the incisal edges of her upper and lower incisors, entirely due to her abnormal method of swallowing. Each time she swallows she shoots forward her lower jaw until her incisors meet edge to edge. This separates her back teeth through which the sides of her tongue protrude. She has a close bite and it is possible that the close bite is due to the pressure of her tongue which is thrust constantly between her molar and premolar teeth.

The duration and intensity of systemic disease and the age at which it occurred can inhibit the growth of the jaws and from my observation it is in the early years of life that more harm is done. The growth of the jaws from birth to 3 years of age is nearly as much as in all the subsequent years put together. A severe hindrance to growth in the early years leaves a mark from which the jaws seldom recover.

The influence of local factors on the growth of the jaws and alignment of the teeth varies a great deal with the resistance of the individual. Thumb sucking can do untold damage where the resistance is poor, and very little damage in the really healthy growing child. The same applies to premature extraction of deciduous teeth, especially in the lower jaw.

It is a common practice to send models of a case to an orthodontist for an opinion. The orthodontist is expected to diagnose the condition from these models without even having seen the patient and with a very inadequate, if any, history. One is asked to plan a treatment for such cases. I personally am very reluctant to do so. Even the bases of the models are so cut that they can give a completely wrong impression of the inclination of the incisors. The variation of the Frankfort Plane from the horizontal when the child stands erect is so slight that if the bases are cut parallel to the Frankfort Plane one can, at least, visualize the appearance of the teeth in the head. Also models alone do not as a rule give sufficient information of the amount of basal bone present, to say nothing of the fact that they provide no idea of the profile, posture and habits of the patient.

I would summarize the chief points I have made as follows:

- (1) A knowledge of the growth and development of the face and jaws is a necessary basis for an orthodontic diagnosis.
- (2) Statistical analyses of development are valuable in showing the direction of growth but their results should not be rigidly applied to the individual.
- (3) Diagnosis should not be based on one anatomical characteristic alone.
- (4) Differentiation of four groups of ætiological factors is necessary in reaching a diagnosis.
- (5) The patient should be seen before any diagnosis is reached. No diagnosis should be based on models alone.

#### REFERENCES

- 1 HELLMAN, M. (1921) *Dent. Cosmos.*, 63, 608.
- 2 ANGLE, E. H. (1906) *Dent. Items*, 28, 421.
- 3 SIMON, P. W. (1926) *Diagnosis of Dental Anomalies*. Boston.
- 4 LINDER, H. (1931) *Fortschr. Orthod.*, 1, 222.
- 5 BALLARD, C. F. (1948) *Dent. Rec.*, 68, 133.
- 6 TWEED, C. H. (1946) *Amer. J. Orthod.*, 32, 175.
- 7 BRASH, J. C. (1924) *The Growth of the Jaws and Palate. The Genesis and Growth of Deformed Jaws and Palate*. London.
- 8 — (1926) *Dent. Rec.*, 46, 641.
- 9 — (1934) *Edinb. med. J.*, 41, 305.
- 10 CHARLES, W. (1934) *Dent. Rec.*, 55, 297.
- 11 RUSHTON, M. (1948) *Dent. Rec.*, 68, 80.
- 12 BROADBENT, B. H. (1943) *See Salzmann*, 1943.
- 13 — (1941) Univ. Penn. Bicentennial Conference, Philadelphia, p. 31.
- 14 — (1943) *See Dewey and Anderson*, 1943.
- 15 DEWEY, M., and ANDERSON, G. M. (1943) *Practical Orthodontics*. London.
- 16 FRIEL, S. (1945) *Proc. R. Soc. Med.*, 38, 456.
- 17 SALZMANN, J. A. (1943) *Principles of Orthodontics*. Philadelphia, p. 235.
- 18 TURNER, J. G. (1948) *Brit. dent. J.*, 84, 1.
- 19 HEMLEY, S. (1944) *Fundamentals of Occlusion*. Philadelphia, p. 136.
- 20 BRODIE, A. G. (1946) *Angle Orthodontist*, 16, 84.
- 21 RIX, E. R. (1946) *Dent. Rec.*, 66, 103.

normal left upper urinary tract, with no concentration of dye up to two hours on the right side. A ureteric catheter meeting impassable obstruction at 7 cm., exploration was decided upon. The ureter, exposed extraperitoneally, was found to be considerably dilated, and to pass under a large transversely disposed vein, which took the place of the right common iliac vein. The arterial distribution was normal. I have not been able to find an exact parallel in the literature, but it is easy to see from a consideration of the development of the abdominal veins how such a condition arose. Considerable plastic exudate rendered the dissection difficult, and it soon became apparent that to attempt to isolate the ureter medial to the venous anomaly would be hazardous. Accordingly, the ureter was sectioned lateral to its disappearance under the vein, and a uretero-neocystostomy was effected in the manner to be described later. In order to avoid tension on the anastomosis, the bladder was drawn up and fixed to the lateral pelvic wall with silk. The patient promptly became asymptomatic (despite some temporary urinary leakage). Unfortunately no subsequent urograms have been obtainable. It is a moot point whether the technique adopted was that of choice, or whether the bladder flap method of Boari, which I propose to discuss later, might not have been preferable in such a high ureteric section.

Another type of congenital abnormality of the ureter which might well come in for injury at the hands of the gynaecologist is that of the pelvic ectopic kidney. I have met with this variant six times. One patient had congenital absence of the vagina, complete urinary incontinence and a number of other congenital defects.

#### Operative Accidents

These resolve themselves into two main groups: (a) Those recognized at the time of operation. (b) Those only discovered late when renal pain, infective phenomena or the development of fistulae make the diagnosis plain.

(a) In the operative group the commonest is the *cut ureter*. It has been customary with gynaecologists to ligate the proximal end of the tube should it be sectioned accidentally, and many proudly state that they have carried out this procedure on several occasions without ill-effects. Such a solution can very, very rarely be justifiable to-day, as was so ably emphasized by Lord Webb-Johnson in 1935. It can achieve its avowed object—namely an aseptic pressure necrosis of the corresponding kidney—only if that organ is initially undilated and uninfected, and that is precisely the kidney that should be preserved. Should it perchance be a solitary kidney the result would be calamitous. The correct procedure, I feel, should be an immediate anastomosis of the severed ureter over a No. 7 or 8 Ch. rubber catheter. The ureteric ends should be trimmed off obliquely, one end of the catheter passed upwards into the renal pelvis, the other downwards into the bladder, and the anastomosis effected by means of four interrupted sutures of 000 plain catgut on an atraumatic curved needle. These should be loosely tied over a small pad of fat. (All sutures in the ureter or renal pelvis should be very loosely tied.) After extraperitonealization of the suture line, a drain is placed appropriately. The bladder should be put at rest with an indwelling catheter, and both this and the splinting ureteric catheter left in ten to fourteen days. It is a simple matter for the urologist to remove the splinting catheter with cystoscopic forceps. I have met with two cases where this technique was successfully employed.

CASE I.—1941: Right nephrectomy for a calculous pyonephrosis. 1945: Admitted with anuria of two days' duration. Flat film disclosed a date-stone shadow in the line of the left upper ureter. Ureteric catheter impinged on this shadow but failed to pass. On exploration of left upper ureter, marked peri-nephritis and peri-ureteritis made exposure difficult. The ureter was isolated well below the level of the obstruction and elevated with tape. Whilst tracing the ureter upwards with sharp dissection, undue traction on the tape led to complete section of this solitary ureter. The patient was enormously stout, so uretero-ureteral anastomosis by the above technique was effected, not without difficulty. No post-operative urinary leakage occurred, and the catheters were removed in fourteen days. A subsequent urogram showed a relatively normal kidney. He was seen this week, three and a half years post-operatively, and unfortunately, though not unexpectedly, has developed a further calculus. The blood urea reading remains normal.

CASE II.—This was a case of an enormous retroperitoneal lipoma operated upon by a general surgeon. In the course of a difficult operation the left ureter was sectioned, and the accident recognized. Immediate anastomosis by the above technique was effected. The patient made an uninterrupted recovery, but no follow-up was possible as he soon left for foreign parts.

Where the ureter is sectioned low in the pelvis, as will usually be the case in gynaecological accidents, it may be preferable to reimplant the ureter into the bladder. A great variety of

and a single row of sutures to bury the ureter in the colon, 4 or 5 interrupted to be precise. Others have departed even farther from the Coffey concept, and employ a direct anastomosis—end-to-side. Only the future can supply the answer to this problem of safe uretero-colic union.

### *Congenital Abnormalities of the Ureter*

I propose to consider the congenital abnormalities of the ureter under two headings: First, those likely to be of diagnostic difficulty; secondly, those likely to confront the gynaecologist with hazards at operation. Of the former group, we have seen a number, such as, supernumerary or ectopic ureters opening into the urethra or vagina and causing persistent incontinence. Some we have met with have been labelled hysterics, others have undergone plastic operations on a bladder neck presumed to be incompetent, and the results have, of course, been unsatisfactory. All cases of persistent congenital urinary incontinence are in urgent need of full urological investigation, including intravenous urography and thorough endoscopic study.

The speaker here showed a slide of a kidney removed from a young woman who had undergone two laparotomies for right iliac fossa pain. At the first intervention she lost her appendix, at the second, a tube. An eminent gynaecologist saw her three times following a sudden profuse discharge of pus from the vagina, to find on all examinations no cause for the symptom. A third laparotomy disclosed a large pyo-ureter opening into the vagina; two ureters were present on the right side, one, relatively normal, leading into the bladder, the other ending in the vagina. Earlier co-operation between urologist and gynaecologist would have saved this patient much.

The congenital ureteric anomalies of interest or hazard to the gynaecologist at operation are the supernumerary ureter, the megal-ureter and the retro-caval distribution. Supernumerary ureters are a relatively common anomaly, being present, in point of fact, in 3-5% of cases. They can prove of considerable importance in the execution of a Wertheim hysterectomy, as has been pointed out by Bonney and others. The megal-ureter is usually redundant, and so tortuous, and may well come in for damage from a carelessly placed suture, or indeed be injured during dissection of a broad-ligament tumour where excessive bleeding may obscure the field. I have met with a number of such damaged ureters. The dilated and tortuous tube may pass unrecognized, especially if, by virtue of its tortuosity, it presents in an abnormal position.

*Intravenous urograms.*—Some radiologists employ compression in the iliac fossæ to effect stasis in the lower ureters, and so secure a denser urographic picture. These dense pictures may give misleading readings if control pictures are not taken without compression.

*Congenital megal-ureter.*—If this condition is diagnosed early, i.e. before the age of 5, a pre-sacral neurectomy will effect a cure, as evidenced by marked diminution in the size of the ureter, a point stressed by Learmonth. If, however, the condition is only recognized later, when irreversible fibrotic changes have occurred, sympathetic surgery is unlikely to give lasting results, and we must seek other therapeutic measures. Louis Michon of Paris has recorded a very fine result lasting over ten years from a lateral anastomosis between ureter and bladder. I have employed this technique on some seven occasions with gratifying results, on the whole. The ureter does not appear to become completely normal, but the renal function is improved and pain disappears. Reflux, too, is non-existent or minimal.

A slide was then shown of a kidney removed for a persistent uretero-vaginal fistula three months after a hysterectomy:

The original operation was a difficult and bloody one, and some ten days post-operatively a uretero-vaginal fistula developed. Early intervention was decided against, and hopes were raised on two occasions by a temporary cessation of the leak. Intravenous urography two and a half months later showed a normal left upper tract, with a poorly functioning right kidney and evident tortuous and dilated ureter. Exploration was made through a lateral extraperitoneal abdominal approach, to be described later. After finding a hugely dilated ureter with acute kinking in its upper portion and marked pelvic dilatation, a nephrectomy was performed.

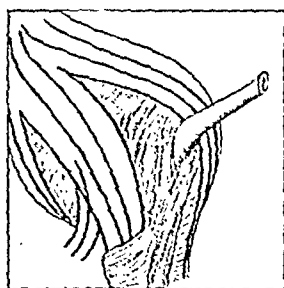
We were evidently dealing here with a congenital megal-ureter damaged during a hysterectomy.

The true postcaval type of ureteric anomaly is of little interest to this Paper, but the variants of this congenital abnormality, in which the ureter lies behind the great veins of the pelvis, are of importance. I have met with two of these. One harboured a sizable and fixed calculus, requiring open operation. The other was discovered when we were called in to deal with a ureter ligatured during a hysterectomy. This latter case is instructive:

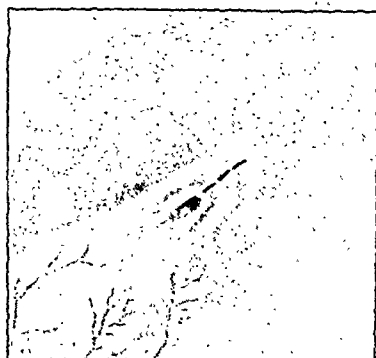
The operating surgeon was unaware of having damaged either ureter, but the development of severe right renal pain in the immediate post-operative period, and the finding of a tender enlarged right kidney, suggested the possibility. The pain was severe, not yielding to analgesics, and pyrexia was minimal. Intravenous urography showed a

for some time, and technically the reparative procedure is difficult with the inevitable plastic exudate following the extensive stripping of the posterior abdominal wall. Considerable oozing is the rule, and moreover these tissues are in no fit state to deal with even minimal infection. Some authorities advise waiting six months before attempting reparative ureteric surgery in such cases, others say three months. My experience suggests that where one has to wait such a period the chances of securing a satisfactorily functioning uninfected kidney are remote, and that, provided intravenous urography reveals a good contralateral kidney, a nephrectomy as soon as the patient's condition warrants it will be the best procedure. It will rid her earlier of the intolerable dampness, and permit a speedier and more comfortable convalescence.

In those cases of fistulae following pelvic operations other than the Wertheim procedure, having decided on early intervention, the next problem besetting the surgeon is the type of operation to employ, and whether the ureter should be exposed intra- or extra-peritoneally. Some earlier authorities, notably Legueu and Thomson-Walker, advocated a routine intra-peritoneal approach, but to-day the consensus of opinion is for the extraperitoneal route. The damage to the ureter has usually occurred 3-6 cm. from the bladder when it has followed abdominal surgery, and closer to the bladder when it has ensued from a vaginal hysterectomy. Theoretically, in the higher lesions it might appear more practical to effect a uretero-ureteral anastomosis, but in practice the lower distal portion of the ureter is usually embedded in scar tissue resulting from the fistulous track, and the best procedure in most cases will be a reimplantation into the bladder. Where the ureter reaches the juxta-trigonal portion of the bladder without tension, the technique already outlined may be adopted. An alternative procedure, and one that appeals to me even more on theoretical grounds, is the transmeatal technique used successfully by Patton (fig. 3).



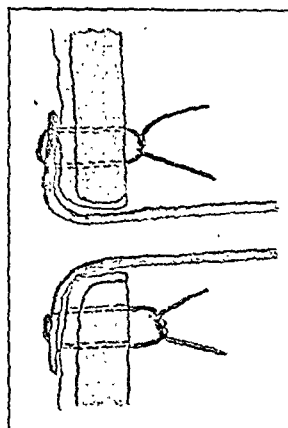
A.



B.



C.



D.

FIG. 3.—Transmeatal neocystostomy. (After Patton.)

A. Diagram showing decussation of detrusor muscle fibres about ureteric insertion. B. Transvesical enlargement of meatus. C. Transvesical view of ureteric fixation. D. Diagram of ureteric fixation.

techniques has been proposed and practised for this, but the following procedure has served me best; it is very similar to that recently described and advocated by Dodson. It must be appreciated that in performing a neo-cystostomy in the female, the submucosal trough method, so generally employed in uretero-colic anastomosis, is wellnigh impossible owing to the thinness of the bladder muscularis, and a short Witzel type of burying is necessary, due care being taken to avoid any compression of the ureter. The value of a splinting catheter for a minimum of ten days is now widely recognized in all reparative surgery of the ureter. The Cummings' nephrostomy catheter we have found most useful for this purpose. Its use is well illustrated in the sketch (fig. 2) and is, I think, original with us. Careful follow-up studies of uretero-neo-cystostomy are badly required to assess end-results.

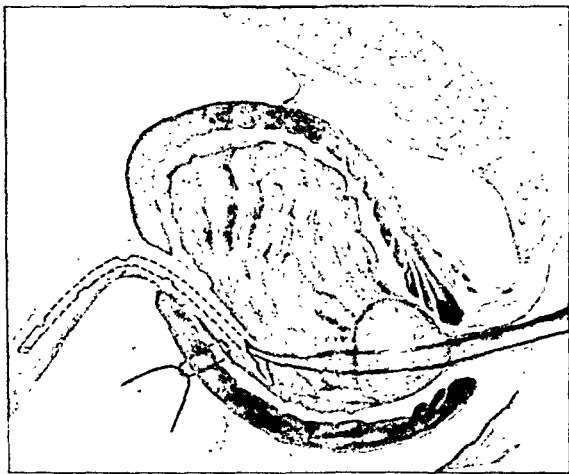


FIG. 2.—Author's use of Cummings' nephrostomy tube in neo-cystostomy.

of forms, e.g. painful hydronephroses due to aseptic ligature, pyonephroses due to infection developing in a ligated or otherwise damaged ureter, or, most commonly, as fistulae either uretero-vaginal or uretero-cutaneous.

Where a hydronephrosis has occurred due to ureteric ligature it is remarkable what recovery will take place when the ligature is removed even several weeks later. In one personal case dealt with three weeks after such a ligature, the ureter was the size of small gut. A uretero-neo-cystostomy was performed, and three months later the intravenous urograms were virtually normal.

An infected kidney will usually require a nephrectomy.

### *Fistulae*

The commonest variety encountered is the uretero-vaginal. The diagnosis is easy, but the treatment offers certain problems. A small proportion will heal spontaneously, either without help or by means of an indwelling ureteric catheter. I have met with 3 cases of spontaneous closure, but one of these proceeded to stricture formation and infected hydronephrosis, necessitating a nephrectomy within eighteen months. The other two remain well with periodic ureteric dilatations. I have only once succeeded in passing a ureteric catheter on the affected side in such a case, and by leaving this in for ten days (with a change on the fifth day) effected a closure. The patient was later lost sight of.

Realizing then that some of such fistulae will close spontaneously, the first problem is *when to advise operation*, and I can but state that I now advise operation early, i.e. before stenosis has occurred leading to upper tract dilatation and infection. It is usually possible to pass a catheter through the fistula and carry out bacteriological and pyelographic studies of the kidney. It has been estimated by Merenyi that 75% of uretero-vaginal fistulae lead ultimately to a nephrectomy, but one cannot help feeling that with modern methods of diagnosis, the use of antibiotics, blood transfusion, &c., and earlier surgical attack on these cases, a high proportion of these kidneys can be saved. The one reservation I maintain to early reparative surgery is the patient who has developed a unilateral uretero-vaginal fistula following a Wertheim hysterectomy. Such a patient may not be fit for further major surgery

Where the ureter has been accidentally ligatured and the situation is recognized during operation, probably all that is necessary is to untie the ligature and place an extraperitoneal drain down to the site lest subsequent leakage occur.

Where the ureter has been caught in a clamp, the treatment will depend on the extent of the clamping. If it is but partial, it will probably only be necessary to place an extraperitoneal drain as though a ureterotomy had been performed, as late sloughing will probably lead to temporary urinary leakage. If the clamping has been complete, it will be best to excise the crushed area and, trimming off each end obliquely, perform an end-to-end anastomosis, as already described.

(b) *Late cases*.—These may present themselves in a variety

was removed by hysterotomy leaving the placenta in situ. As soon as the placenta separated and came away there occurred a prompt subsidence of the ureteric dilatation.

This upper tract dilatation in pregnancy is of great clinical importance in that the stasis predisposes to urinary tract infections, which are sometimes, even with modern antiseptics, difficult to clear up until after term. In pre-mandelic and pre-sulphonamide days the indwelling ureteric catheter could be virtually life-saving, and certainly saved many a foetus, but I have not had occasion to use this method during the past ten years.

#### *The Ureter in Pelvic Inflammations and Benign Tumours*

I have been unable to find any exhaustive statistics on the incidence of upper tract dilatation in this connexion, but a perusal of several small series would appear to show the following approximate figures:

|                                          |    |    |     |
|------------------------------------------|----|----|-----|
| Pelvic inflammatory conditions           | .. | .. | 60% |
| Fibroids { large, i.e. above pelvic brim | .. | .. | 66% |
| { small                                  | .. | .. | 30% |
| Ovarian cyst                             | .. | .. | 40% |

What improvement occurs when the pelvic lesion has been dealt with appropriately? Of 30 reported cases exhibiting previous upper tract dilatation and studied post-operatively, only 43.3% showed return to complete normality, 30% partial regression and 26.7% no change. A high proportion of those in which failure to regress was noted were in the inflammatory group.

From a consideration of these facts I would make a plea for more extensive use of intravenous urography pre- and post-operatively in gynaecological pelvic lesions, for a selective use of ureteric dilatation may save many a kidney, or prevent recurrent renal infections.

#### *The Ureter in Genital Prolapse*

Several investigators have reported on the incidence of upper urinary tract dilatation in this connexion. The figures vary from 50–80% in severe degrees of prolapse. Such an incidence would appear to call for an invariable intravenous urogram in all cases of extensive prolapse. If dilatation is present, a repeat urogram should be made three months post-operatively to ascertain if the urinary tract has returned to normal. If not, urological treatment may be indicated. The ureter is occasionally injured during the performance of a vaginal repair for prolapse. One or both ureters may be caught in carelessly placed sutures, or the development of a hæmatoma may compress the lower end of both ureters, and lead to anuria. In one well-known case in which an anuria followed a colporrhaphy, reopening of the wound and removal of sutures led to a prompt re-establishment of the urinary flow. I shall detail later a personal case in which a similar accident occurred, and in which a different procedure was adopted (Case II, p. 44).

#### *The Ureter in Carcinoma of the Cervix*

Williams in 1895 showed that autopsies of patients dying of Ca. cervicis showed an 85% incidence of dilated upper urinary tracts. Graves and Kickham in 1936 reported that of 257 patients suffering from carcinoma of the cervix, 123 or 50% were found either on urological investigation or at autopsy to have dilated upper tracts. Of 87 patients autopsied, 79% were found to have sufficient dilatation to produce renal insufficiency. Jaffe, Meigs and co-workers reported in 1940 that of 390 such patients from their clinic, 70% had obstruction to one or both ureters. Despite such findings too few gynaecologists seem to appreciate the desirability of urological investigation in these cases. The pre-operative presence of ureteric dilatation would appear to be of grave prognostic significance, as indeed it is in vesical neoplasms. It indicates a lateral spread of the growth into the broad ligaments. The post-operative finding of ureteric dilatation may betoken either a recurrence of the growth or peri-ureteric fibrosis. The latter may be amenable to periodic ureteric stretching. Dilatation occurring during radiation therapy may be merely a reactionary oedema and be temporary. Post-radiation dilatation is apparently relatively common, as I have come across many such cases. There are several reported cases from the post-mortem rooms where death has been due to renal failure caused by ureteric obstruction from post-radiation fibrosis, with no evidence of a recurrence of the malignant process.

In such cases where increasing ureteric obstruction is developing, urological help is indicated. Ureteric dilatation, neo-cystostomy, ureterostomy, nephrostomy and intestinal transplantation all have their place.

I have already stressed the advantage in being aware of the presence of a supernumerary ureter before embarking on a Wertheim's hysterectomy.

It would appear then that all cases of carcinoma of the cervix should be investigated urologically pre- and post-operatively. Closer co-operation between the two specialties should lead to improved results in dealing with this all too common disease.



I have never had occasion to employ this technique,<sup>1</sup> but bearing in mind the decussation of the muscular fibres of the detrusor in the neighbourhood of the ureteric orifices, and the minimal risk of fibrosis from scarring, the method would appear to be sound. In either of these techniques it is essential to have the ureter reaching the bladder without tension, and the device advocated by Dodson of mobilizing the ureter and straightening its course, i.e. obliterating the pelvic curve, already mentioned, is worthy of note.

Where the ureteric damage is high, or sloughing has occurred, some other manœuvre must be employed, and the vesical flap method first described by Boari in 1894 experimenting on dogs, and subsequently successfully used in man by Demel, Rohde, Ockerblad, Flocks and Caughlan, can give most satisfactory results.

Another technique which has been successfully employed in a few cases, e.g. by Neuswanger and Higgins, is an end-to-side uretero-ureteral anastomosis, i.e. suturing the proximal end of the damaged ureter into the side of its fellow. This would appear to carry the risk of jeopardizing the good ureter and kidney and should be condemned. An intestinal transplantation would be preferable. I have not had occasion to resort to such a transplant in a case of uretero-vaginal fistula, but the procedure has been adopted in America for a uretero-vaginal fistula following a vaginal hysterectomy. I cannot help thinking that the indications for such a transplant in these fistulae must be rare.

On one occasion only have I resorted to a uretero-colic anastomosis for a ureteric lesion following gynaecological intervention. An inexperienced surgeon performed a supravaginal hysterectomy for a broad ligament fibroid, and damaged the ureter in the region of the infundibulo-pelvic ligament. Appreciating his error he repaired the ureter and lapped it with peritoneum. Faulty drainage was employed, and an intraperitoneal urinary leakage ensued, necessitating the reopening of the abdomen and the establishment of extraperitoneal drainage some days later. When the case was seen some weeks afterwards in consultation, a uretero-cutaneous fistula was present with considerable ureteric dilatation. Owing to high sloughing of the ureter, vesical anastomosis was not feasible, and the ureter was transplanted into the descending colon, with a satisfactory result.

In a number of these cases of uretero-vaginal fistulae the urologist may find himself in some doubt as to whether to carry out a nephrectomy or whether to attempt some form of reparative surgery. This will be particularly likely to happen when some time has been allowed to elapse between the original injury and the proposed intervention, and ureteric and pelvic dilatation have occurred. When I find myself in such doubt I resort to the following tactics. I expose the lower ureter through a Gibson type of incision extraperitoneally and study the area of damage. If reparative surgery is decided upon this can be perfectly well effected through such an incision, though my incision of election for exposure of the lower end of the ureter is a mid-line one. In the doubtful case, this lateral incision has the advantage that with a minimal enlarging upward it is relatively easy to effect a nephrectomy should such appear to be indicated at operation. The procedure entails but a single incision, which heals well with careful suturing. I have employed this manœuvre on five occasions, when in doubt. In three a nephrectomy was performed, in two reparative surgery of the ureter. When such pre-operative doubt does not exist, the elective incisions will be a mid-line sub-umbilical for lower ureteric surgery, and a classical sub-costal for a nephrectomy.

#### *The Ureters in Pregnancy*

It has long been recognized that upper tract dilatation occurs in pregnancy though the precise mechanism has remained in some doubt. The earliest concept was a purely mechanical one, but such is not the whole answer. The hormone theory next held sway, and it was shown that injection of progesterone would lead to softening and atony of the ureters. The hormone theory, however, did not explain the common increased dilatation on the right side. Many investigators have worked on the problem, and using Trattner's hydrophorograph have been able to demonstrate the atony and diminished peristaltic movements antedating the dilatation. The present-day view is that, as a rule, during the first two months of pregnancy there is no alteration in the ureters. From the third month onwards, thanks to the increased progesterone circulating, there is a softening and a diminished peristalsis which render the ureters liable to the pressure effects of the gravid uterus. Owing to the more common dextro-rotation of this organ the brunt of the pressure is on the right ureter, and the dilatation is mainly above the brim of the pelvis. In most cases there is little or no dilatation of the lower third of the ureter. In support of this is the observation that there is no dilatation of the ureter or pelvis of the pelvic ectopic kidney, and that dilatation does not occur in eight species of four-footed animals studied. van Wageningen and Jenkins working on Rhesus monkeys found that the upper tract dilatation did not subside when the foetus

<sup>1</sup>Since writing the above I have employed the transmeatal technique with extreme satisfaction in a case of uretero-vaginal fistula following an abdominal hysterectomy.

Cystography revealed no reflux. It is remarkable what complete recovery the left kidney has made when one realizes that it secreted no urine for fifteen days. It also raises the possibility of a reflex anuria developing after the commonly adopted practice of tying off a severed ureter.

CASE III.—This illustrates another type of anuria, evidently reflex in character, of which I have met quite a number of examples.

A young woman of 28 had an incomplete miscarriage at the fourth month. The remnants were curetted. Following this, complete anuria developed. Intravenous therapy, splanchnic block, spinal anaesthesia, &c., were all tried without avail. Her life was despaired of. I saw her five and a half days after the onset of the anuria. The blood urea was over 200 mg.%; she was comatose, with parched tongue, sordes around lips, &c. The picture was very grave. A rapid decapsulation of one kidney was carried out, and renal secretion restarted with ultimate complete recovery. Not unexpectedly a parotitis developed during the post-operative period. This patient, a young and valuable life, was literally snatched from the jaws of death.

I have employed renal decapsulation for anuria on 14 occasions, with 10 successes and 4 deaths. 2 of the latter were hopeless when seen, one grossly septic following a criminal abortion, the other grossly cachectic from extensive gastric carcinoma for which a palliative gastrectomy was performed with resulting anuria. Of the other 2 deaths, one followed post-partum bleeding for which many transfusions had been given, and she succumbed within a few hours of a bilateral decapsulation, her pre-operative condition being very serious. The fourth death was in a woman who developed a secondary hæmorrhage following a colpo-perineorrhaphy. She was given a transfusion and anuria followed. The usual medical measures for blood incompatibility failing, I carried out a decapsulation which resulted in a recommencement of urinary secretion, but after two days of evident improvement urinary output again stopped, and she succumbed. Subsequent investigation suggested the probability that we were dealing here with a Rhesus incompatibility.

I am aware that my proportion of successes with decapsulation in anuria is higher than those reported by most, though not all, other writers, but I attribute this largely to the technique adopted enabling us to carry out a rapid operation with minimal shock. The patient is laid face downwards with the table broken or bridge slightly elevated. Either local or light general anaesthesia is employed. The lower pole of each kidney is exposed in turn through an incision along the outer border of each erector spinae. The aponeurosis incised, the fatty capsule is opened, revealing the lower pole of the kidney. No attempt is made to deliver the kidney, but the true capsule is nicked, the opening enlarged with scissors and rapidly stripped back from the parenchyma with the finger. As much as possible is resected to prevent the development of a "Goldblatt kidney" by compression of the renal vessels by the rolled back capsule. A small corrugated drain is left down to the kidney to take care of the ooze; the aponeurosis is approximated with 4 points of catgut and the skin closed. The bilateral procedure can be completed in ten to twelve minutes.

Two points I would mention in connexion with this operation: It is noteworthy in these cases how the renal parenchyma will bulge through the nick in the true capsule, showing clearly the strangulating effect of the inelastic capsule. I saw this particularly well in 2 cases of post-scarlatinal glomerulo-nephritis treated thus successfully for anuria. Whether the relief of the intrarenal tension by this manoeuvre, or the partial sympathectomy effected by the decortication causes the re-establishment of the urinary secretion, is not certain.

The second point I should like to make in this connexion is the fact that I most strongly advocate a bilateral decortication. In 3 cases in which we carried out a unilateral procedure, though the urinary output promptly recommenced, the diuresis was not so marked, and consequently the uræmic manifestations disappeared less quickly than in the cases in which we carried out a bilateral operation.

To summarize the care of these most important anuric cases:

(1) Take an accurate case-history from attendant observers, paying particular attention to the possibility of damage to one or both ureters.

(2) Have complete blood chemistry estimations in the hope of being able to correct faulty electrolytic balance, and also of assessing the urgency with which intervention need be counselled.

(3) Do not flood the patient with intravenous fluids and overtax the poorly functioning kidney.

(4) Search for any evidence of ureteric obstruction, e.g. tender, enlarged kidney.

(5) Do not waste time if conservative measures are failing, but advocate early exploration of the upper ureters and kidneys. Proceed then *secundum artem*.

*Anuria*

This group represents one of the most interesting in the whole range of that "No Man's Land" between urology and gynaecology. Many of these cases are in young people doomed to die from renal failure if not adequately treated. As mentioned earlier we know personally of 3 who succumbed and proved *post mortem* to have been amenable to surgical cure. We count certain survivals following intervention, after being given up as hopeless by eminent medical authorities, as amongst our greatest surgical triumphs. Certain groups are, of course, now well known, chiefly those following excessive sulphur therapy, and the treatment is established: search of any urine procurable, even a c.c. or two, for evidence of the tell-tale crystals; early cystoscopy with careful examination of the ureteric orifices for evidence of the sulphur sludge; catheterization of the ureters to dislodge this sludge and allow pelvic drainage with prompt administration of alkaline intravenous therapy. These measures may re-establish the renal flow and avert uræmia. Where ureteric catheterization is impossible, pyelostomy should be carried out, combined, I believe, with renal decapsulation lest intrarenal tubular blockage has occurred, or alternatively a shunt, as described by Trueta, which may well be helped by the partial sympathetic block resulting from the decapsulation.

Lesser-known varieties of anuria are even more important in this present Paper and a careful history-taking will, as ever, be amply repaid. One has to determine whether the cessation of urinary output is pre-renal or post-renal. The nature of the supposed underlying cause will be helpful in attempting to establish this differentiation. Where doubt exists after history-taking and clinical examination, a prompt recourse to surgery will often be warranted, as will be instanced presently. A rapid examination of the upper ureter will be the key to the problem. If it is dilated, then we are dealing with a post-renal obstructive phenomenon; if it is not dilated, then we have a pre-renal lesion to contend with. In the former a ureterostomy or nephrostomy will relieve the obstruction and be life-saving; in the latter, a prompt decapsulation is most likely to yield satisfactory dividends, though beneficial results have on occasion followed splanchnic block, spinal analgesia, &c. The tactics adopted in a variety of anuric cases may be interesting and instructive.

CASE I.—This lady was seen in consultation twenty-eight hours after a straightforward supra-vaginal hysterectomy. No urine had been secreted since the operation, and the patient exhibited the clinical picture of a concealed hæmorrhage. No tenderness was present in either loin. The most probable diagnosis was a retroperitoneal hæmatoma compressing the ureters. This was confirmed by cystoscopy—the large blue mass of the hæmatoma being visible through the thin-walled bladder. Incidentally I have never seen this method of diagnosis mentioned in the literature. The abdomen was reopened, the hæmatoma evacuated and drained, and urinary secretion promptly restarted with complete recovery.

I have already mentioned three similar cases of retroperitoneal hæmatoma due to slipped ligature causing anuria, and only discovered at autopsy.

CASE II.—This case I saw in consultation three days following an anterior and posterior repair. No urine had been passed since the operation. The attendant observers had diagnosed anuria twenty-four hours post-operatively, and intravenous therapy was instituted. When seen, there was profound anorexia, dry tongue and an enlarged and tender right kidney; no abnormal findings in the left renal region. No hæmatoma was palpable on vaginal or rectal examination, nor was any detected on cystoscopy. The marked distortion and œdema of the trigone precluded a view of either orifice, so ureteric catheterization was impossible. The blood urea reading was 97 mg.%. The choice here lay between removing the anterior vaginal sutures in the hope of freeing the ureters, presumably compressed, without a certainty of success, or of relieving the right kidney, evidently blocked, by direct approach. The second alternative was selected. The right loin was explored, and a hugely dilated ureter containing dark blood-stained urine was found. This was opened, and the urine escaped under great pressure. An 18 F. rubber urethral catheter was introduced along the ureter into the renal pelvis and brought out on to the skin. Urinary excretion being re-established, the blood urea dropped to 23 mg.% in forty-eight hours. Two weeks later, as no urine had as yet entered the bladder, a further cystoscopy was made to ascertain if ureteric catheterization was yet possible, but neither orifice could be visualized. The following day the lower end of both ureters was exposed by a mid-line extraperitoneal approach. The left ureter appeared normal. It was incised, no urine escaped, and a catheter readily passed through the orifice. The right ureter was still markedly dilated, and a ligature was found encircling the tube in its juxta-vesical portion. This ureter was cut across proximally and re-implanted into the bladder. The ligature of the right ureter had evidently caused a reflex anuria on the left side. Intravenous urography, four months later, showed a completely normal left upper urinary tract and but slight dilatation of the right renal pelvis.

Cystography revealed no reflux. It is remarkable what complete recovery the left kidney has made when one realizes that it secreted no urine for fifteen days. It also raises the possibility of a reflex anuria developing after the commonly adopted practice of tying off a severed ureter.

CASE III.—This illustrates another type of anuria, evidently reflex in character, of which I have met quite a number of examples.

A young woman of 28 had an incomplete miscarriage at the fourth month. The remnants were curetted. Following this, complete anuria developed. Intravenous therapy, splanchnic block, spinal anaesthesia, &c., were all tried without avail. Her life was despaired of. I saw her five and a half days after the onset of the anuria. The blood urea was over 200 mg.%; she was comatose, with parched tongue, sordes around lips, &c. The picture was very grave. A rapid decapsulation of one kidney was carried out, and renal secretion restarted with ultimate complete recovery. Not unexpectedly a parotitis developed during the post-operative period. This patient, a young and valuable life, was literally snatched from the jaws of death.

I have employed renal decapsulation for anuria on 14 occasions, with 10 successes and 4 deaths. 2 of the latter were hopeless when seen, one grossly septic following a criminal abortion, the other grossly cachectic from extensive gastric carcinoma for which a palliative gastrectomy was performed with resulting anuria. Of the other 2 deaths, one followed post-partum bleeding for which many transfusions had been given, and she succumbed within a few hours of a bilateral decapsulation, her pre-operative condition being very serious. The fourth death was in a woman who developed a secondary haemorrhage following a colpo-perineorrhaphy. She was given a transfusion and anuria followed. The usual medical measures for blood incompatibility failing, I carried out a decapsulation which resulted in a recommencement of urinary secretion, but after two days of evident improvement urinary output again stopped, and she succumbed. Subsequent investigation suggested the probability that we were dealing here with a Rhesus incompatibility.

I am aware that my proportion of successes with decapsulation in anuria is higher than those reported by most, though not all, other writers, but I attribute this largely to the technique adopted enabling us to carry out a rapid operation with minimal shock. The patient is laid face downwards with the table broken or bridge slightly elevated. Either local or light general anaesthesia is employed. The lower pole of each kidney is exposed in turn through an incision along the outer border of each erector spinae. The aponeurosis incised, the fatty capsule is opened, revealing the lower pole of the kidney. No attempt is made to deliver the kidney, but the true capsule is nicked, the opening enlarged with scissors and rapidly stripped back from the parenchyma with the finger. As much as possible is resected to prevent the development of a "Goldblatt kidney" by compression of the renal vessels by the rolled back capsule. A small corrugated drain is left down to the kidney to take care of the ooze; the aponeurosis is approximated with 4 points of catgut and the skin closed. The bilateral procedure can be completed in ten to twelve minutes.

Two points I would mention in connexion with this operation: It is noteworthy in these cases how the renal parenchyma will bulge through the nick in the true capsule, showing clearly the strangulating effect of the inelastic capsule. I saw this particularly well in 2 cases of post-scarlatinal glomerulo-nephritis treated thus successfully for anuria. Whether the relief of the intrarenal tension by this manoeuvre, or the partial sympathectomy effected by the decortication causes the re-establishment of the urinary secretion, is not certain.

The second point I should like to make in this connexion is the fact that I most strongly advocate a bilateral decortication. In 3 cases in which we carried out a unilateral procedure, though the urinary output promptly recommenced, the diuresis was not so marked, and consequently the uraemic manifestations disappeared less quickly than in the cases in which we carried out a bilateral operation.

To summarize the care of these most important anuric cases:

(1) Take an accurate case-history from attendant observers, paying particular attention to the possibility of damage to one or both ureters.

(2) Have complete blood chemistry estimations in the hope of being able to correct faulty electrolytic balance, and also of assessing the urgency with which intervention need be counselled.

(3) Do not flood the patient with intravenous fluids and overtax the poorly functioning kidney.

(4) Search for any evidence of ureteric obstruction, e.g. tender, enlarged kidney.

(5) Do not waste time if conservative measures are failing, but advocate early exploration of the upper ureters and kidneys. Proceed then *secundum artem*.

*Anuria*

This group represents one of the most interesting in the whole range of that "No Man's Land" between urology and gynaecology. Many of these cases are in young people doomed to die from renal failure if not adequately treated. As mentioned earlier we know personally of 3 who succumbed and proved *post mortem* to have been amenable to surgical cure. We count certain survivals following intervention, after being given up as hopelessly by eminent medical authorities, as amongst our greatest surgical triumphs. Certain groups are, of course, now well known, chiefly those following excessive sulphur therapy, and the treatment is established: search of any urine procurable, even a c.c. or two, for evidence of the tell-tale crystals; early cystoscopy with careful examination of the ureteric orifices for evidence of the sulphur sludge; catheterization of the ureters to dislodge this sludge and allow pelvic drainage with prompt administration of alkaline intravenous therapy. These measures may re-establish the renal flow and avert uræmia. Where ureteric catheterization is impossible, pyelostomy should be carried out, combined, I believe, with renal decapsulation lest intra-renal tubular blockage has occurred, or alternatively a shunt, as described by Trueta, which may well be helped by the partial sympathetic block resulting from the decapsulation.

Lesser-known varieties of anuria are even more important in this present Paper and a careful history-taking will, as ever, be amply repaid. One has to determine whether the cessation of urinary output is pre-renal or post-renal. The nature of the supposed underlying cause will be helpful in attempting to establish this differentiation. Where doubt exists after history-taking and clinical examination, a prompt recourse to surgery will often be warranted, as will be instanced presently. A rapid examination of the upper ureter will be the key to the problem. If it is dilated, then we are dealing with a post-renal obstructive phenomenon; if it is not dilated, then we have a pre-renal lesion to contend with. In the former a ureterostomy or nephrostomy will relieve the obstruction and be life-saving; in the latter, a prompt decapsulation is most likely to yield satisfactory dividends, though beneficial results have on occasion followed splanchnic block, spinal analgesia, &c. The tactics adopted in a variety of anuric cases may be interesting and instructive.

CASE I.—This lady was seen in consultation twenty-eight hours after a straightforward supra-vaginal hysterectomy. No urine had been secreted since the operation, and the patient exhibited the clinical picture of a concealed hæmorrhage. No tenderness was present in either loin. The most probable diagnosis was a retroperitoneal hæmatoma compressing the ureters. This was confirmed by cystoscopy—the large blue mass of the hæmatoma being visible through the thin-walled bladder. Incidentally I have never seen this method of diagnosis mentioned in the literature. The abdomen was reopened, the hæmatoma evacuated and drained, and urinary secretion promptly restarted with complete recovery.

I have already mentioned three similar cases of retroperitoneal hæmatoma due to slipped ligature causing anuria, and only discovered at autopsy.

CASE II.—This case I saw in consultation three days following an anterior and posterior repair. No urine had been passed since the operation. The attendant observers had diagnosed anuria twenty-four hours post-operatively, and intravenous therapy was instituted. When seen, there was profound anorexia, dry tongue and an enlarged and tender right kidney; no abnormal findings in the left renal region. No hæmatoma was palpable on vaginal or rectal examination, nor was any detected on cystoscopy. The marked distortion and œdema of the trigone precluded a view of either orifice, so ureteric catheterization was impossible. The blood urea reading was 97 mg.%. The choice here lay between removing the anterior vaginal sutures in the hope of freeing the ureters, presumably compressed, without a certainty of success, or of relieving the right kidney, evidently blocked, by direct approach. The second alternative was selected. The right loin was explored, and a hugely dilated ureter containing dark blood-stained urine was found. This was opened, and the urine escaped under great pressure. An 18 F. rubber urethral catheter was introduced along the ureter into the renal pelvis and brought out on to the skin. Urinary excretion being re-established, the blood urea dropped to 23 mg.% in forty-eight hours. Two weeks later, as no urine had as yet entered the bladder, a further cystoscopy was made to ascertain if ureteric catheterization was yet possible, but neither orifice could be visualized. The following day the lower end of both ureters was exposed by a mid-line extraperitoneal approach. The left ureter appeared normal. It was incised, no urine escaped, and a catheter readily passed through the orifice. The right ureter was still markedly dilated, and a ligature was found encircling the tube in its juxta-vesical portion. This ureter was cut across proximally and re-implanted into the bladder. The ligature of the right ureter had evidently caused a reflex anuria on the left side. Intravenous urography, four months later, showed a completely normal left upper urinary tract and but slight dilatation of the right renal pelvis.

Cystography revealed no reflux. It is remarkable what complete recovery the left kidney has made when one realizes that it secreted no urine for fifteen days. It also raises the possibility of a reflex anuria developing after the commonly adopted practice of tying off a severed ureter.

CASE III.—This illustrates another type of anuria, evidently reflex in character, of which I have met quite a number of examples.

A young woman of 28 had an incomplete miscarriage at the fourth month. The remnants were curetted. Following this, complete anuria developed. Intravenous therapy, splanchnic block, spinal anaesthesia, &c., were all tried without avail. Her life was despaired of. I saw her five and a half days after the onset of the anuria. The blood urea was over 200 mg. %; she was comatose, with parched tongue, sordes around lips, &c. The picture was very grave. A rapid decapsulation of one kidney was carried out, and renal secretion restarted with ultimate complete recovery. Not unexpectedly a parotitis developed during the post-operative period. This patient, a young and valuable life, was literally snatched from the jaws of death.

I have employed renal decapsulation for anuria on 14 occasions, with 10 successes and 4 deaths. 2 of the latter were hopeless when seen, one grossly septic following a criminal abortion, the other grossly cachectic from extensive gastric carcinoma for which a palliative gastrectomy was performed with resulting anuria. Of the other 2 deaths, one followed post-partum bleeding for which many transfusions had been given, and she succumbed within a few hours of a bilateral decapsulation, her pre-operative condition being very serious. The fourth death was in a woman who developed a secondary hæmorrhage following a colpo-perineorrhaphy. She was given a transfusion and anuria followed. The usual medical measures for blood incompatibility failing, I carried out a decapsulation which resulted in, a recommencement of urinary secretion, but after two days of evident improvement urinary output again stopped, and she succumbed. Subsequent investigation suggested the probability that we were dealing here with a Rhesus incompatibility.

I am aware that my proportion of successes with decapsulation in anuria is higher than those reported by most, though not all, other writers, but I attribute this largely to the technique adopted enabling us to carry out a rapid operation with minimal shock. The patient is laid face downwards with the table broken or bridge slightly elevated. Either local or light general anaesthesia is employed. The lower pole of each kidney is exposed in turn through an incision along the outer border of each erector spinæ. The aponeurosis incised, the fatty capsule is opened, revealing the lower pole of the kidney. No attempt is made to deliver the kidney, but the true capsule is nicked, the opening enlarged with scissors and rapidly stripped back from the parenchyma with the finger. As much as possible is resected to prevent the development of a "Goldblatt kidney" by compression of the renal vessels by the rolled back capsule. A small corrugated drain is left down to the kidney to take care of the ooze; the aponeurosis is approximated with 4 points of catgut and the skin closed. The bilateral procedure can be completed in ten to twelve minutes.

Two points I would mention in connexion with this operation: It is noteworthy in these cases how the renal parenchyma will bulge through the nick in the true capsule, showing clearly the strangulating effect of the inelastic capsule. I saw this particularly well in 2 cases of post-scarlatinal glomerulo-nephritis treated thus successfully for anuria. Whether the relief of the intrarenal tension by this manœuvre, or the partial sympathectomy effected by the decortication causes the re-establishment of the urinary secretion, is not certain.

The second point I should like to make in this connexion is the fact that I most strongly advocate a bilateral decortication. In 3 cases in which we carried out a unilateral procedure, though the urinary output promptly recommenced, the diuresis was not so marked, and consequently the uræmic manifestations disappeared less quickly than in the cases in which we carried out a bilateral operation.

To summarize the care of these most important anuric cases:

(1) Take an accurate case-history from attendant observers, paying particular attention to the possibility of damage to one or both ureters.

(2) Have complete blood chemistry estimations in the hope of being able to correct faulty electrolytic balance, and also of assessing the urgency with which intervention need be counselled.

(3) Do not flood the patient with intravenous fluids and overtax the poorly functioning kidney.

(4) Search for any evidence of ureteric obstruction, e.g. tender, enlarged kidney.

(5) Do not waste time if conservative measures are failing, but advocate early exploration of the upper ureters and kidneys. Proceed then *secundum artem*.

## SUMMARY

The ureter is worthy of more careful attention by the gynaecologist than it has hitherto been accorded. Urologists must advocate a more widespread use of intravenous urography, both pre- and post-operatively, in cases of large benign pelvic tumours, pelvic inflammations, genital prolapse and cervical carcinomata. By pre-operative employment, the gynaecologist will obtain much useful information as to the disposition and configuration of that elusive tube, the ureter, and so the better avoid its operative injury. He will also improve his ability to prognosticate in cases of cervical carcinoma. The post-operative use of intravenous urography will enable him to assess whether his urological colleague should be called in to assist in expediting the recovery of a damaged kidney, or, indeed, of saving such an organ. Our own urological house, too, must be put in order. Urologists should, by a more careful follow-up of cases, assess better the end-results of the various types of ureteric anastomoses, and so put on a sounder basis the treatment of ureteric lesions, traumatic and otherwise.

In operative injuries of the ureter which are recognized at the time, conservative surgery is best, with uretero-ureteral, uretero-vesical or uretero-colic anastomosis, in that order of preference, rather than a proximal ureteric ligature.

In uretero-vaginal and uretero-cutaneous fistulae early operation should usually be entertained, as procrastination leads frequently to stenosis, dilatation, infection and irreparable damage to the corresponding kidney, necessitating a probable later nephrectomy. Even in cases of spontaneous closure of such fistulae, follow-up ureteric dilatations will usually be necessary.

The treatment of anuria has been briefly discussed, and the role played by the ureter, in deciding between ureterostomy and renal decapsulation, has been considered.

## REFERENCES

- ABESHOUSE, B. S. (1945) *J. Urol.*, 53, 27.  
 BARNES, R., and FARLEY, S. (1948) *J. Urol.*, 59, 466.  
 BEER, E. (1933) *Amer. J. Surg.*, 20, 8, 27.  
 BOARI, A. (1894) *Atti Accad. Sci. med. nat. Ferrara*, 48, 149.  
 CAUGHLAN, G. V. (1947) *J. Urol.*, 58, 428.  
 DEMEL, R. (1946) *Zbl. Chir.*, 51, 2001.  
 DODSON, A. I. (1946) *J. Urol.*, 55, 225.  
 FLOCKS, R. H. (1947) *J. Canad. med. Ass.*, 55, 514.  
 GRAVES, R. C., and KICKHAM, C. J. E. (1936) *J. Urol.*, 36, 618.  
 HIGGINS, C. C. (1935) *J. Urol.*, 34, 349.  
 JAFFE, H. L., and MEIGS, J. V. (1940) *Surg. Gynec. Obstet.*, 70, 178.  
 LORD, J. W., JR., STEFKO, PAUL L., and STEVENS, A. R. (1943) *J. Urol.*, 49, 249.  
 MERENYI, I. (1948) *Acta Urol.*, 2, 58.  
 NEUSWANGER, C. H. (1936) *New Engl. J. Med.*, 215, 653.  
 OCKERBLAD, N. F. (1947) *J. Urol.*, 57, 845.  
 PATTON, J. F. (1939) *J. Urol.*, 42, 1021.  
 ROHDE, C. (1937) *Zbl. Chir.*, 64, 409.  
 VAN WAGENEN, G., and JENKINS, R. H. (1939) *J. Urol.*, 42, 1010.  
 WEBB-JOHNSON, A. (1935) *Lancet* (i), 1083.  
 WILLIAMS, R. (1895) *Brit. Gynec. J.*, 11, 529.

[November 25, 1948]

The following cases and specimens were shown:

- Cystic Disease of the Kidney in a Baby aged 12 Months.—Mr. J. H. CARVER.  
 Renal Trauma in Children (2 Cases).—Mr. ASHTON MILLER.  
 Nephrocalcinosis (X-rays).—Mr. A. W. BADENOCH.  
 Angioma of Kidney.—Mr. EDGAR FRESHMAN.  
 Wilms' Tumour in a Child Aged 2½ Years.—Mr. F. R. KILPATRICK.  
 Anaplastic Carcinoma of Kidney.—Mr. GEOFFREY PARKER.  
 Anuria in a Solitary Kidney after Uretero-intestinal Anastomosis.—Mr. HOWARD G. HANLEY.  
 Unusual Form of Vesical Papilloma.—Mr. D. St.C. L. HENDERSON.  
 Chronic Non-Specific Granulomatous Prostatitis.—Dr. W. St.C. SYMMERS for Mr. HUGH DONOVAN.  
 Rhabdomyosarcoma of the Prostate.—Mr. J. C. ANDERSON.  
 Diverticulum of Urethra.—Mr. ROBERT COX.  
 Carcinoma of Urethra.—Mr. H. K. VERNON.  
 Bowen's Disease of Glans Penis.—Mr. R. D. WILKINS for Mr. H. K. VERNON.  
 Seminoma of Abdominal Testis.—Mr. J. SCHOLEFIELD.  
 Rhabdomyosarcoma in a Teratoma of Testis, with Co-existing Seminoma.—Mr. I. H. GRIFFITHS.

# Section of Epidemiology and State Medicine

President—Sir ALLEN DALEY, M.D., F.R.C.P., D.P.H., K.H.P.

[October 4, 1948]

## DISCUSSION ON POLIOMYELITIS—ENGLAND AND WALES

Dr. A. H. Gale: *The Evolution of Epidemic Poliomyelitis in England and Wales.*

An excuse is needed for adding to the enormous literature of poliomyelitis and it cannot be claimed that this paper throws any new light on the mysterious features of the epidemiology of the disease but there are a few points of special interest about the evolution of the disease in its epidemic form in this country. In view of the experience of 1947, which was an entirely new one, it seems justifiable to review them. A brief general account of the epidemic of 1947 has already been given elsewhere (Gale, 1948).

### THE STATISTICAL RAW MATERIAL

It must be admitted that the statistical raw material is even more unsatisfactory than it is for most other communicable diseases and that its defects are to a large extent due to the nature of the disease and not to ignorance or omissions on the part of doctors. The returns from the hospital survey (Bradley and Gale, 1948) showed that among 6,762 patients admitted to hospital with a diagnosis of poliomyelitis or polioencephalitis the diagnosis was subsequently confirmed in about 70%. If patients are to be admitted to hospital early this order of error of original diagnosis is probably inevitable. The errors of notification statistics are well known but since 1940 an attempt has been made to remove some of them. The figures published in the Registrar-General's weekly return are derived from the original notifications sent in by general practitioners and this notification often has to be sent in when the diagnosis is still in doubt. In times of epidemic there is a natural tendency to notify cases on suspicion more readily than when the disease is not particularly prevalent. The Quarterly Returns contain figures derived from the returns of "corrected" notifications which are sent to the Registrar-General every quarter by the Medical Officers of Health of individual sanitary districts. Even these are subject to errors in that there are different views as to what clinical picture justifies a notification of poliomyelitis. This point will arise again in considering fatality rates.

Statistics of notifications and of deaths for the whole country are available from the latter part of 1912 and, in the early years from 1912-19, the Local Government Board made inquiries about individual cases so that for those years there is some information about age distribution, and about the incidence of paralysis and of deaths among notified cases. For the early years there are also several very valuable reports on individual outbreaks made by medical officers of the Local Government Board. Sources used for general reviews have been Batten's Lumleian Lectures for 1916, the Annual Report of the Medical Officer Local Government Board 1915-16, MacNalty (1927) on "Epidemic Diseases of the Nervous System" and the Annual Reports of the Chief Medical Officer of the Ministry of Health, particularly those for 1926 and 1938.

### CHANGES IN INCIDENCE—GENERAL AND LOCAL

In 1896 Pasteur reported 7 cases in one family. Badham (1836) had described 4 cases at Worksop in 1835 but he did not say whether they were associated with one another and so this incident cannot be called an epidemic. From 1896, then to Treves' account of an outbreak at Upminster in 1908, there were several accounts of little groups of cases apparently associated and there was some evidence of sporadic cases in the big towns. Parker recorded the first outbreak of any size in Bristol in 1909 when there were 37 paralytic cases. In 1909 the special reports of the medical officers of the Local Government Board began and Farrar reported on the 1910 outbreaks in rural districts chiefly in Leicestershire and in Dorset. The years 1911-13 also appear to have been years of high incidence and it was in 1911 that the well-known epidemic occurred in Devon and Cornwall. It has been said that 1911 was the year in which epidemics really began to occur and that the very hot summer had something to do with it but, though 1911 was a bad year, epidemics began in



1909 or 1910. It has also been said that these early epidemics were all in rural areas but Bristol, Plymouth, Carlisle and Barrow-in-Furness all had substantial outbreaks in this early period of 1909-13. After 1913 there seems to have been a period of relatively low incidence and it is not until the outbreak in Surrey in 1917 described by MacNalty (1918) that the special reports began again.

After the first world war there were references to small outbreaks of poliomyelitis in most of the Annual Reports of the Chief Medical Officer of the Ministry of Health but the years 1926 and 1938 stood out from other years. In neither of them did the incidence in the country as a whole approach that of 1947 but in a few areas incidence was probably as high as it was in the areas of maximum incidence in 1947. The epidemic of 1947 was remarkable rather for its wide distribution than for very high local incidence.

In some of the early epidemics there seems to have been a very high incidence of paralytic cases in quite small areas—one example is the village of Cerne, Dorset, in 1910 with a population of about 600 and 15 paralytic cases, another the outbreak in the Broadstairs schools of 1926.

The distribution of cases early in 1947 suggested rather that an endemic disease—endemic particularly in the big centres of population—became epidemic, rather than that a new strain was imported from elsewhere. This point requires further investigation as it is possible that a new strain may have been imported in previous years and lain latent until conditions were particularly favourable for epidemic spread.

There is evidence that the proportion of cases in rural areas rose a little during the epidemic. The proportion of notifications in rural districts rose from 12% in the first quarter to 23% in the fourth quarter of 1947 and the same in the first quarter of 1948. In the past there has been no great difference in urban and rural incidence but in the epidemic years 1926 and 1938 rural incidence was a little higher than urban.

#### FATALITY RATES

Where special inquiries have been made the number of deaths is smaller than one would expect from the Registrar-General's figures based on death certificates. There is not a great deal to go on but if the Registrar-General's figures for 1912-13 are compared with those obtained through the special enquiry made into individual cases by the Local Government Board there were nearly twice as many deaths in the Registrar-General's figures as were found by the Local Government Board inquiries, and this in spite of the fact that the Local Government Board managed to get particulars of a high percentage of notified cases. The actual figures for the two years 1912-13 together were: Cases investigated by Local Government Board 1,559—deaths 213. Registrar-General's figures: Cases notified 1,583, deaths certified 386. Bradley and Gale (1948) found rather the same thing in their hospital enquiry in 1947. It was estimated that the enquiry included about 75% of the notified cases and there were 360 deaths in the sample—say 450 as the expected figure for the whole country for the period. 506 deaths were certified in the first three-quarters of 1947 which was nearly the same period as that covered by the hospital survey. There are many possible contributory causes of this but perhaps one of importance is that an appreciable number of deaths from obscure nervous diseases occur every year and that poliomyelitis and polioencephalitis get a share of them just as encephalitis lethargica does.

#### CHANGE IN AGE-INCIDENCE

The generally accepted view is that in civilized countries the age-incidence of the disease has been rising in the past thirty years but it has been suggested that this change is only apparent and is due to the change in the age-constitution of the population and to the increased reporting of non-paralytic cases. There is no very comprehensive information on age distribution in this country but one can make some comparison between the experience of 1912-13 and that of 1947; the comparison is not entirely satisfactory but I think it is fairly convincing. The method adopted has been to take the cases in each age-group, divide by the estimated population at that age and so calculate two series of age-specific morbidity rates. The next step is to express the rate at 0-5 as 100 and the rates in the other age-groups as percentages of it. Using this method it is found that in 1912-13 the rate at 5-10 was 17% of that at 0-5, that at 10-15 was 8% and that at 15-30 was 2%. In 1947, however, the rate at 5-10 was 84% of that at 0-5, that at 10-15 was 62% and that at 15-25 was 36%. A similar result is obtained by comparing the incidence of paralysis in different age-groups in the 1912-13 cases and in the hospital survey for 1947.

There is some evidence that as the epidemic of 1947 progressed there was a slight shift of cases to older age-groups. In the second quarter of 1947 9% of the cases were over 25, in the third 16%, in the fourth 18% and in the first quarter of 1948 24%. The proportion at 5-15 remained fairly constant at about 35% but the proportion in age-group 0-5 fell from 35% to 20%.

## CLINICAL TYPE

There is one interesting small point in the clinical descriptions of the very early cases and that is that cranial nerve palsies were described very early, for Badham mentions a squint as occurring in one of his cases in 1835. Pasteur (1896) described one case with a right hemiplegia and transient paralysis of the right side of the face and another case with a transient squint.

The proportion of cases with some degree of permanent paralysis in the Local Government Board cases in 1912-13 was 52.7% and in the hospital survey of 1947 39% were classed as having moderate or severe paralysis likely to cause permanent disability. The two classifications are not quite comparable as it seems probable that some of those with mild paralysis in 1947 may have some slight permanent paralysis.

The following two points are put forward for discussion:

(1) That the distribution of notifications in the early stages does suggest that an endemic disease became epidemic rather than that a new strain was imported.

(2) That from the epidemiological point of view some kind of herd immunity seems to develop in an epidemic even though the evidence obtained from the studies of antibody content of the blood is so difficult and conflicting.

## REFERENCES

- Rep. med. Offr. loc. Govt. Bd.* (1915-16) Appendix 4.  
 BADHAM, J. (1836) *Lond. Med. Gaz.*, N.S., 17, 215.  
 BATTEN, F. E. (1911) *Public Health*, 25, 51.  
 — (1916) *Lumleian Lectures, Brain*, 39, 115.  
 BRADLEY, W. H., and GALE, A. H. (1948) *Mon. Bull. Minist. Hlth. Publ. Hlth. Lab. Ser.*, 7, 56.  
 FARRAR, R. (1912) *Rep. Loc. Govt. Bd. Pub. Hlth and Med. Subj.*, N.S., No. 61, p. 87.  
 GALE, A. H. (1948) *Mon. Bull. Minist. Hlth. Publ. Hlth. Lab. Ser.*, 7, 127.  
 MACNALLY, A. S. (1918) *Rep. Loc. Govt. Bd. Pub. Hlth. and Med. Subj.*, N.S., No. 120, 1.  
 — (1927) *Epidemic Diseases of the Nervous System*, London.  
 PASTEUR, W. (1896-97) *Trans. Chir. Soc. London*, 30, 143.  
 PARKER, G. (1911) *Brit. med. J.* (i), 609.  
 REECE, R. J. (1912) *Rep. Loc. Govt. Bd. Pub. Hlth. and Med. Subj.*, N.S., No. 61, p. 10.  
 TREVES, W. W. (1909) *Brain*, 32, 285.

Dr. Allan M. McFarlan, Reader in Human Ecology, University of Cambridge:

*The Epidemiology of Poliomyelitis in England and Wales in 1947. Field Studies, including a preliminary report on a survey organized by the Public Health Laboratory Service which is directed by the Medical Research Council for the Ministry of Health.*

Ecology has been defined as a branch of biology dealing with living organisms' habits, modes of life and relations to their surroundings. "Human ecology" therefore includes social studies by economists and town planners as well as the "disciplines" (Ryle, 1948) of social medicine and social pathology, and uses the methods devised by many workers in the many fields which contribute to epidemiology. The scope of the medical part of human ecology might well be defined in the terms which Hirsch (1883) applied to the science which he called geographical and historical pathology "a science... which will give: firstly, a picture of the occurrence, the distribution, and the types of the diseases of mankind, in distinct epochs of time, and at various points of the earth's surface; and, secondly, will render an account of the relations of those diseases to the external conditions surrounding the individual and determining his manner of life". In 1927 Frost quoted this sentence as an admirable expression of the aims of epidemiology and drew attention to the implication that epidemiology is essentially an inductive science, concerned not merely with describing the distribution of disease but equally or more with fitting it into a consistent philosophy (see Frost, 1941).

A similar trend of thought is to be found in Greenwood's Linacre Lecture (1943) where he considers the results of experimental studies of epidemics in herds of mice (Greenwood *et al.*, 1936) and then describes the plan of campaign of the statistical epidemiologists of the Johns Hopkins School of Public Health who were inspired largely by Frost. "They leave the experimental work to Nature, but acquaint themselves thoroughly with the characters of herds in which Nature will make experiments, families of human beings, rich and poor, well housed and ill housed. The precise statistical characterization of human groups is no new thing. One remembers the work of Booth and Rowntree. It is a question merely of a change of emphasis; the epidemiologists interest themselves primarily in those group characters which might be expected to have a bearing on the rise and fall of epidemic diseases and do not disdain to record 'trifling' ailments. This is slow, tedious work, but, in my submission, it is neither less important nor makes fewer demands on intellectual ability than experimental medicine in the laboratory sense of the term; but its prestige in popular or even scientific circles is far less."

1909 or 1910. It has also been said that these early epidemics were all in rural areas but Bristol, Plymouth, Carlisle and Barrow-in-Furness all had substantial outbreaks in this early period of 1909-13. After 1913 there seems to have been a period of relatively low incidence and it is not until the outbreak in Surrey in 1917 described by MacNalty (1918) that the special reports began again.

After the first world war there were references to small outbreaks of poliomyelitis in most of the Annual Reports of the Chief Medical Officer of the Ministry of Health but the years 1926 and 1938 stood out from other years. In neither of them did the incidence in the country as a whole approach that of 1947 but in a few areas incidence was probably as high as it was in the areas of maximum incidence in 1947. The epidemic of 1947 was remarkable rather for its wide distribution than for very high local incidence.

In some of the early epidemics there seems to have been a very high incidence of paralytic cases in quite small areas—one example is the village of Cerne, Dorset, in 1910 with a population of about 600 and 15 paralytic cases, another the outbreak in the Broadstairs schools of 1926.

The distribution of cases early in 1947 suggested rather that an endemic disease—endemic particularly in the big centres of population—became epidemic, rather than that a new strain was imported from elsewhere. This point requires further investigation as it is possible that a new strain may have been imported in previous years and lain latent until conditions were particularly favourable for epidemic spread.

There is evidence that the proportion of cases in rural areas rose a little during the epidemic. The proportion of notifications in rural districts rose from 12% in the first quarter to 23% in the fourth quarter of 1947 and the same in the first quarter of 1948. In the past there has been no great difference in urban and rural incidence but in the epidemic years 1926 and 1938 rural incidence was a little higher than urban.

#### FATALITY RATES

Where special inquiries have been made the number of deaths is smaller than one would expect from the Registrar-General's figures based on death certificates. There is not a great deal to go on but if the Registrar-General's figures for 1912-13 are compared with those obtained through the special enquiry made into individual cases by the Local Government Board there were nearly twice as many deaths in the Registrar-General's figures as were found by the Local Government Board inquiries, and this in spite of the fact that the Local Government Board managed to get particulars of a high percentage of notified cases. The actual figures for the two years 1912-13 together were: Cases investigated by Local Government Board 1,559—deaths 213. Registrar-General's figures: Cases notified 1,583, deaths certified 386. Bradley and Gale (1948) found rather the same thing in their hospital enquiry in 1947. It was estimated that the enquiry included about 75% of the notified cases and there were 360 deaths in the sample—say 450 as the expected figure for the whole country for the period. 506 deaths were certified in the first three-quarters of 1947 which was nearly the same period as that covered by the hospital survey. There are many possible contributory causes of this but perhaps one of importance is that an appreciable number of deaths from obscure nervous diseases occur every year and that poliomyelitis and polioencephalitis get a share of them just as encephalitis lethargica does.

#### CHANGE IN AGE-INCIDENCE

The generally accepted view is that in civilized countries the age-incidence of the disease has been rising in the past thirty years but it has been suggested that this change is only apparent and is due to the change in the age-constitution of the population and to the increased reporting of non-paralytic cases. There is no very comprehensive information on age distribution in this country but one can make some comparison between the experience of 1912-13 and that of 1947; the comparison is not entirely satisfactory but I think it is fairly convincing. The method adopted has been to take the cases in each age-group, divide by the estimated population at that age and so calculate two series of age-specific morbidity rates. The next step is to express the rate at 0-5 as 100 and the rates in the other age-groups as percentages of it. Using this method it is found that in 1912-13 the rate at 5-10 was 17% of that at 0-5, that at 10-15 was 8% and that at 15-30 was 2%. In 1947, however, the rate at 5-10 was 84% of that at 0-5, that at 10-15 was 62% and that at 15-25 was 36%. A similar result is obtained by comparing the incidence of paralysis in different age-groups in the 1912-13 cases and in the hospital survey for 1947.

There is some evidence that as the epidemic of 1947 progressed there was a slight shift of cases to older age-groups. In the second quarter of 1947 9% of the cases were over 25, in the third 16%, in the fourth 18% and in the first quarter of 1948 24%. The proportion at 5-15 remained fairly constant at about 35% but the proportion in age-group 0-5 fell from 35% to 20%.

## CLINICAL TYPE

There is one interesting small point in the clinical descriptions of the very early cases and that is that cranial nerve palsies were described very early, for Badham mentions a squint as occurring in one of his cases in 1835. Pasteur (1896) described one case with a right hemiplegia and transient paralysis of the right side of the face and another case with a transient squint.

The proportion of cases with some degree of permanent paralysis in the Local Government Board cases in 1912-13 was 52.7% and in the hospital survey of 1947 39% were classed as having moderate or severe paralysis likely to cause permanent disability. The two classifications are not quite comparable as it seems probable that some of those with mild paralysis in 1947 may have some slight permanent paralysis.

The following two points are put forward for discussion:

(1) That the distribution of notifications in the early stages does suggest that an endemic disease became epidemic rather than that a new strain was imported.

(2) That from the epidemiological point of view some kind of herd immunity seems to develop in an epidemic even though the evidence obtained from the studies of antibody content of the blood is so difficult and conflicting.

## REFERENCES

- Rep. med. Offr. loc. Govt. Bd.* (1915-16) Appendix 4.  
 BADHAM, J. (1836) *Lond. Med. Gaz.*, N.S., 17, 215.  
 BATTEN, F. E. (1911) *Public Health*, 25, 51.  
 — (1916) Lumenian Lectures, *Brain*, 39, 115.  
 BRADLEY, W. H., and GALE, A. H. (1948) *Mon. Bull. Minist. Hlth. Publ. Hlth. Lab. Ser.*, 7, 56.  
 FARRAR, R. (1912) *Rep. Loc. Govt. Bd. Pub. Hlth. and Med. Subj.*, N.S., No. 61, p. 87.  
 GALE, A. H. (1948) *Mon. Bull. Minist. Hlth. Publ. Hlth. Lab. Ser.*, 7, 127.  
 MACNALLY, A. S. (1918) *Rep. Loc. Govt. Bd. Pub. Hlth. and Med. Subj.*, N.S., No. 120, 1.  
 — (1927) *Epidemic Diseases of the Nervous System*, London.  
 PASTEUR, W. (1896-97) *Trans. Chir. Soc. London*, 30, 143.  
 PARKER, G. (1911) *Brit. med. J.* (i), 609.  
 REECE, R. J. (1912) *Rep. Loc. Govt. Bd. Pub. Hlth. and Med. Subj.*, N.S., No. 61, p. 10.  
 TREVES, W. W. (1909) *Brain*, 32, 285.

Dr. Allan M. McFarlan, Reader in Human Ecology, University of Cambridge:

*The Epidemiology of Poliomyelitis in England and Wales in 1947. Field Studies, including a preliminary report on a survey organized by the Public Health Laboratory Service which is directed by the Medical Research Council for the Ministry of Health.*

Ecology has been defined as a branch of biology dealing with living organisms' habits, modes of life and relations to their surroundings. "Human ecology" therefore includes social studies by economists and town planners as well as the "disciplines" (Ryle, 1948) of social medicine and social pathology, and uses the methods devised by many workers in the many fields which contribute to epidemiology. The scope of the medical part of human ecology might well be defined in the terms which Hirsch (1883) applied to the science which he called geographical and historical pathology "a science... which will give: firstly, a picture of the occurrence, the distribution, and the types of the diseases of mankind, in distinct epochs of time, and at various points of the earth's surface; and, secondly, will render an account of the relations of those diseases to the external conditions surrounding the individual and determining his manner of life". In 1927 Frost quoted this sentence as an admirable expression of the aims of epidemiology and drew attention to the implication that epidemiology is essentially an inductive science, concerned not merely with describing the distribution of disease but equally or more with fitting it into a consistent philosophy (see Frost, 1941).

A similar trend of thought is to be found in Greenwood's Linacre Lecture (1943) where he considers the results of experimental studies of epidemics in herds of mice (Greenwood *et al.*, 1936) and then describes the plan of campaign of the statistical epidemiologists of the Johns Hopkins School of Public Health who were inspired largely by Frost. "They leave the experimental work to Nature, but acquaint themselves thoroughly with the characters of herds in which Nature will make experiments, families of human beings, rich and poor, well housed and ill housed. The precise statistical characterization of human groups is no new thing. One remembers the work of Booth and Rowntree. It is a question merely of a change of emphasis; the epidemiologists interest themselves primarily in those group characters which might be expected to have a bearing on the rise and fall of epidemic diseases and do not disdain to record 'trifling' ailments. This is slow, tedious work, but, in my submission, it is neither less important nor makes fewer demands on intellectual ability than experimental medicine in the laboratory sense of the term; but its prestige in popular or even scientific circles is far less."

Greenwood emphasized the statistical part of epidemiology but both he and Frost recognized the fundamental importance of the field or clinical epidemiologist. Like Copeman (1948) they recognized how much good work in epidemiology is done by "amateurs". Snow won fame as an anaesthetist (Richardson, 1900) as well as for his work on cholera (Underwood, 1948). Budd was a busy physician as well as an investigator of typhoid fever (Goodall, 1936). Nathan Smith who investigated typhoid fever in Connecticut (Paul, 1930) also performed the second ovariectomy in the U.S.A., wrote about his method of amputating at the knee-joint and built up medical schools at Dartmouth and Yale. More recently Pickles (1939) has shown that a country practice offers opportunities for most valuable epidemiological work.

Epidemiological studies may thus be carried out by an "amateur" of genius, but to-day there is often need for a team in which the field worker collaborates with workers in bacteriological or virus laboratories and with statisticians. This is particularly true in poliomyelitis (e.g. Seddon *et al.*, 1946).

#### THE PLAN OF A FIELD SURVEY IN ENGLAND AND WALES IN 1947

At the request of Sir Wilson Jameson, Chief Medical Officer of the Ministry of Health, an investigation of poliomyelitis was started in Oxford in September 1947. Professor H. J. Seddon undertook the clinical work. Mr. T. H. Cotton and the Staff of the Nuffield Bureau of Health and Sickness Records drew up a survey form to collect data in a manner suitable for machine analysis. The Medical Officers of Health in Berkshire, Buckinghamshire and Oxfordshire did the necessary laborious field work and returned the forms to Dr. G. T. Cook of the Public Health Laboratory Service in Oxford. Dr. Cook scrutinized the forms and assisted in field investigations. The results of this part of the survey are described on page 52.

With the co-operation of many Medical Officers of Health and of Directors of Laboratories in the Public Health Laboratory Service the survey was extended to some areas in the north-west, east and south-west of England and to parts of Wales. These forms were scrutinized at Cambridge and combined with the Oxford forms for analysis there with the help of Dr. Ian Sutherland of the Institute of Social Medicine.

#### SOME PRELIMINARY RESULTS

Forms were received concerning 911 cases in which the diagnosis of poliomyelitis was made by the clinician in charge of the case. There were 678 paralytic and 233 non-paralytic cases. The cases were distributed equally in the three age-groups 0-4, 5-14 and over 15 years. Males were more numerous than females in the ratio of 1.3 to 1. In age and sex distribution, therefore, the sample was similar to the larger one of Bradley and Gale's (1948) hospital survey.

*Geographical distribution.*—Spot maps and epidemic curves constructed from the forms received from the various areas gave the impression of a widespread epidemic with a few scattered foci of higher incidence.

In towns it was usual to find a series of cases spread evenly over two or three months and giving a plateau rather than an abrupt curve. In Eccles, however (Sweetnam, 1948), there was an abrupt curve similar to those of the epidemics in Mauritius (McFarlan *et al.*, 1946) and Singapore (McFarlan, 1946), St. Helena (Nissen, 1947) and many other places. In Eccles the abrupt curve was associated with a high attack rate (1.1 per 1,000), a geographical spread and a relatively high proportion (60%) of cases in the 0-4 age-group. Suggestions of a geographical spread were found in spot maps of cases in some other towns. In these towns the cases were spread over several months, and the attack rate and age distribution of cases were similar to those for the country as a whole. The geographical spread in towns is reminiscent of the Melbourne epidemic where spread occurred mainly by abortive cases in children (Merrilees, 1937). In yet other towns there was no evidence of geographical spread; cases occurred all over the town throughout the period of high prevalence with occasional focal concentrations. Daley (1948) found this sort of distribution of cases in London.

In most of the rural areas studied there was a similar wide diffusion of cases without clear indication of geographical spread. In Essex studies were undertaken with the encouragement and help of Dr. W. A. Bullough, Medical Officer of Health, Essex County Council, and of many other M.O.s.H. and in that county there was a suggestion of geographical spread. The weekly notifications for four geographical groups of health districts showed different epidemic curves. In the south-west, which includes boroughs just outside London, many cases occurred in July and the peak incidence was in August; in the south-east and north-east the peak was in September, while in the north-west there were few cases before September and the peak incidence was in October. The available information about 24 cases in relatively isolated villages showed that contact might have been the

mode of infection in 12 instances; in 6 there was a history of direct contact and in 6 others visits of the patient or his associates to London might have been the source of infection. The geographical spread in Essex thus appeared to be due in part to an early or late introduction of infection into localities according to the greater or lesser amount of movement of persons between them and London. Spread from place to place along the lines of human traffic was evident in some parts of the country but was not clearly shown in Essex.

*Incubation period and duration of infectivity.*—In 8 cases there was a history of short exposure to another case. The numbers of days from this exposure to the onset of symptoms were 0, 2, 4, 4, 7, 13, 13, 13. It is possible that some of the cases with short intervals were infected in some other way than by the recorded exposure. The intervals of seven days in one case and thirteen days in 3 others agree with the usual estimate of the incubation period as seven to fourteen days and with the observations of Aycock and Kessel (1943), Casey (1942), Casey *et al.* (1945), McFarlan *et al.* (1946) and Sweetnam (1948).

On the day of exposure one infecting case had had symptoms for one day and another for fifteen days. In the other six infecting cases the apparently effective exposure preceded the onset of symptoms by 1, 3, 3, 3, 4 and 7 days. The patient who apparently infected the case with an incubation period of seven days had had symptoms for fifteen days on the day of contact; the 3 patients who infected cases with incubation periods of thirteen days had no symptoms until one, three and seven days after the day of contact. The presence of virus in the faeces of cases for some weeks after the onset (Horstmann *et al.*, 1944) shows that patients may be infectious for considerable periods. However, the small number of cases presented here and the findings of Aycock and Kessel (1943) and Casey *et al.* (1945) suggest that infectivity is greatest in the incubation period and the early stages of illness, the period at which the virus has been found in the throat.

*Multiple cases in families.*—There were 23 families with 2 cases. In 9 instances the intervals between the onsets of illness were nil to four days, in 11 they were six to ten days, and in 3 they were fourteen, nineteen and thirty-five days respectively. The rapidity with which the virus spreads in families has been evident in several epidemiological studies and has been demonstrated by virus isolation (Zintek, 1947; Brown *et al.*, 1948).

*History of contact with a previous case.*—In the present series of cases contact with a previous case was established in 5.8%. In a further 4.3% of cases there had been indirect contact through another member of the household or a close friend. These percentages might have been higher if full and early investigation had been possible in all cases. When this was so, as in the Essex rural cases already mentioned, a history of contact was obtained in half the cases. In many cases, particularly in towns, direct or indirect contact with carriers was often probable or possible since there were other cases in the vicinity, but the available data did not justify a tabulation in these categories.

*Other possible sources of infection.*—During the three weeks before onset some 42% of cases had been away from their home town for a day or more. This figure reflects the habits of the community during the summer holiday period and can be interpreted as showing that many patients had had contacts outside their usual ones while travelling or on holiday and might have been infected by these contacts. Equally the figure shows that in many cases there was no such possibility. Similar arguments arise from other figures: 25% of the cases had been swimming, 23% had paddled and 39% of patients aged 5 to 14 years had been at Sunday school. The number of flies in the house at the time of onset of illness was said to be *many* in 21%, *few* in 41% and *negligible* in 25%; no estimate being given in 13%. These sources of infection may have been operative in some cases but not in all. Further analysis of these and similar data is in progress. It was not possible to make control inquiries, but the help which they might have given in assessing these results is a strong argument for including them in any future investigation.

Among the figures being analysed are some concerning the possibility of spread by food. The results will be of the sort reported above. Detailed local investigations are necessary to incriminate a foodstuff. Hargreaves (1948) made such investigations in the village of St. Austell in Cornwall and concluded that the virus might have been spread by the cream filling of cakes consumed by all the cases and made in a bakery where two employees were household contacts of two early cases. It is desirable that cases of poliomyelitis should be investigated in the same way as cases of paratyphoid fever, in order to see how frequently faecal contamination of food may be the mode of transmission of the virus. Careful inquiries are necessary because the virus does not multiply in the foodstuff and so is unevenly distributed in it. Food-borne poliomyelitis would not necessarily show the explosive type of outbreak which is often found in food-borne paratyphoid fever. If possible, laboratory work should support epidemiological conclusions by virus isolation from suspected carriers.

*Variations in the severity of paralysis.*—The severity of paralysis may be estimated

(Seddon *et al.*, 1946) by the number of "limbs" involved. Of the 678 paralytic cases 28% had paralysis of three or more limbs. There was an increase in the percentage of these severe paralyses as the epidemic progressed (from 15.6 in June to 43.5 in December) and with increasing age of the patient (from 17.0 at 0-4 years to 51.5 at 15-24 years). In 45 cases with a history of physical and/or mental stress the percentage of severe paralyses was 47. This high percentage is in line with Ritchie Russell's demonstration (1947) of the effect of exercise on the severity of paralysis and reinforces his conclusion that bed-rest may be a valuable measure in the prevention of paralysis in a patient showing signs of meningeal involvement.

**Tonsillectomy.**—No case was recorded as having had a tonsillectomy within four weeks of onset. This may have been due to the virtual cessation of tonsillectomy during the epidemic (Glover, 1948). The incidence of bulbar paralysis was higher in 27 patients whose tonsils had been removed (26%) than in 355 patients whose tonsils were present (8%).

**Social and environmental factors.**—The average age of attack has been found to vary when calculated for groups of cases defined by the occupation of the chief wage earner or certain housing conditions. Further analysis of these figures may elucidate some of the factors which determine the age of attack.

### CONCLUSION

From all the work done in this survey it is likely that no striking discovery will be made and that no new preventive measure will be suggested. The results will, however, be a contribution to the epidemiology or ecology of poliomyelitis. They will at least facilitate comparison of the 1947 epidemic in England and Wales with previous and subsequent epidemics there and in other countries.

### REFERENCES

- AYCOCK, W. L., and KESSEL, J. F. (1943) *Amer. J. med. Sci.*, 205, 454.  
 BRADLEY, W. H., and GALE, A. H. (1948) *Mon. Bull. Min. Hlth. and Publ. Hlth. Lab. Serv.*, 7, 56.  
 BROWN, G. C., FRANCIS, T., AINSLIE, J. (1948) *J. exp. Med.*, 87, 21.  
 CASEY, A. E. (1942) *J. Amer. med. Ass.*, 120, 805.  
 —, FISHBEIN, W. I., BUNDESEN, H. N. (1945) *J. Amer. med. Ass.*, 129, 1141.  
 COPEMAN, W. S. C. (1948) *Proc. R. Soc. Med.*, 41, 502.  
 DALEY, A. (1948) *Proc. R. Soc. Med.*, 41, 52.  
 FROST, W. H. (1941) *Papers of Wade Hampton Frost, M.D.: A Contribution to Epidemiological Method*. New York.  
 GLOVER, J. A. (1948) *Mon. Bull. Min. Hlth. and Publ. Hlth. Lab. Serv.*, 7, 150.  
 GOODALL, E. W. (1936), William Budd. Bristol.  
 GREENWOOD, M. (1943) *Authority in Medicine: Old and New*. London.  
 —, BRADFORD HILL, A., TOPLEY, W. W. C., and WILSON, J. (1936) *Spec. Rep. Ser. med. Res. Coun. Lond.*, No. 209.  
 HARGREAVES, E. R. (1948) M.D. Thesis. University of Cambridge.  
 HIRSCH, A. (1883) *Handbook of Geographical and Historical Pathology* transl. C. Creighton, 1, p. 1. (New Sydenham Society, 106) London.  
 HORSTMANN, D. M., WARD, R., MELNICK, J. L. (1944) *J. Amer. med. Assn.*, 126, 1061.  
 MCFARLAN, A. M. (1946) *J. Roy. Army med. Corps*, 87, 37.  
 —, DICK, G. W. A., SEDDON, H. J. (1946) *Quart. J. Med.*, 15, 183.  
 MERRILEES, C. R. (1937) *Hlth. Bull. Publ. Hlth. Dept. Victoria*, 51, 1414.  
 NISSEN, K. I. (1947) *Proc. R. Soc. Med.*, 40, 923.  
 PAUL, J. R. (1930) *Yale J. Biol. Med.*, 2, 169.  
 PICKLES, W. N. (1939) *Epidemiology in Country Practice*. Bristol.  
 RICHARDSON, B. W. (1900) *Disciples of Æsculapius*, 1, 227. London.  
 RUSSELL, W. R. (1947) *Brit. med. J.* (ii), 1023.  
 RYLE, J. A. (1948) *Changing Disciplines*. London.  
 SEDDON, H. J., HAWES, E. I. B., RAFFRAY, J. R. (1946) *Lancet* (ii), 707.  
 SWEETNAM, W. P. (1948) *Brit. med. J.* (i), 1172.  
 UNDERWOOD, E. A. (1948) *Proc. R. Soc. Med.*, 41, 165.  
 ZINTEK, A. R. (1947) *Amer. J. Hyg.*, 46, 248.

### Dr. G. T. Cook: *Poliomyelitis Survey in the Oxford Region.*

The region consists of the three counties, Berkshire, Buckinghamshire and Oxfordshire. It is a compact region with a total area of a little more than 2,000 square miles and a population of approximately one million. Rather more than a fifth of this number live in the two County Boroughs, Oxford and Reading.

The region contains 53 administrative areas and these are served by 22 Medical Officers of Health, excluding assistants. In order to obtain their co-operation the Medical Officers of Health of all three counties were invited by Dr. E. Donaldson, Senior M.O., Ministry of Health, to a meeting held at the Wingfield-Morris Orthopædic Hospital, Oxford, in

September 1947. The purpose and scope of the survey were explained and copies of the form drawn up by the Nuffield Bureau of Health & Sickness Records were circulated. The collection of the information was to be the responsibility of the Medical Officer of Health and all those present very willingly signified their readiness to help. It was also decided that the Public Health Laboratory at Oxford would form a convenient centre for the distribution and collection of forms. In addition to the completion of the form, there were two other matters which required attention for the efficient working of the scheme. The first of these was arranging some mechanism for the prompt transmission of information about new cases to the laboratory so that any points of interest, such as second cases in households or villages, could be followed up without delay. This was achieved through a system of notification worked out with the Medical Officers of Health. The second was some arrangement by which the assessment of the clinical data of as many cases as possible could be made by the same orthopaedic specialist or a member of his team. Most of the patients were admitted to hospitals in Oxford and these came under the supervision of Professor Seddon; with the co-operation of other hospitals one of his colleagues was also able to examine patients treated elsewhere or have access to their clinical histories.

Much of the information obtained from the forms has been incorporated with the results of the general survey, but there are one or two points of interest which apply particularly to this region. During 1947 168 cases were originally notified as poliomyelitis or polio-encephalitis. Of these, 158 with their onset of disease during that year were confirmed. Clinical details together with information about the date of onset were obtained from 136 out of 158 cases—86%. For 107 of these the epidemiological sections of the form were also completed. Many of the 22 cases for whom no form was returned were taken ill while staying in the region for a short time and had subsequently returned home.

The number of cases in the three counties during 1947 and the attack rates per 100,000 are given below:

|                       | Cases | Attack rate per 100,000 |
|-----------------------|-------|-------------------------|
| Berkshire .. ..       | 65    | 17                      |
| Buckinghamshire .. .. | 40    | 11                      |
| Oxfordshire .. ..     | 53    | 20                      |

In fourteen instances previous direct contact with another case was definite or probable. There were only three households with more than one case; one of these families lived in a small village of some 600 inhabitants where six paralytic and a number of abortive cases occurred. A study of the date of onset of 125 cases for the four months July to October shows a relatively late start of the epidemic in this region compared with some parts of the country. There were more cases in August than in any other month but no well-defined peak was seen for any of the three counties.

Spot-maps illustrating the geographical distribution of cases within the region show that most of the cases occurred in the more populated areas such as Oxford C.B. and the south-east corner of the region nearest to London. By a study of serial spot-maps and the histories an attempt was made to trace the reasons for the distribution of cases in the less thickly populated parts of the region. Where data were available it was found that many of these either had some contact with a previous case or infected area or had probably contracted their infection outside the region. In 9 out of 24 towns or villages with one or more cases it seemed likely that the first or only case had introduced the disease from outside the region. In five of the remainder there was a history of daily visits by a member of the family, usually the father, to an area where cases were occurring. The results are similar to those reported by Dr. McFarlan for rural cases in Essex.

To summarize, during the months July to October cases were first observed in the more populated areas close to London. The numbers here increased fairly rapidly in late July and August and then gradually fell until in October there were very few fresh cases. In the Oxford area sporadic cases occurred from August to October with an increased incidence towards the end of that period. The general picture in the less populated areas appeared to be one of a number of independent scattered foci of infection, some of which were probably introduced from outside the region, rather than a gradual spread from the earlier cases in the south-east.

Mr. B. Benjamin said that, although in the early stages of the 1947 outbreak in London there was some suggestion of a spread from a focus, a number of other foci soon appeared, and the rapid spread throughout the County made the picture too confusing to follow any distinct avenues of spread. The same extension to adult age-groups was experienced as elsewhere in the Country. In the years 1937–1946 78% of London cases were under 15 years of age. In 1947 only 65% were within this age-group. The ratio of male to female cases was 1.2 to 1.



Although the geographical spread within London was not worth following, it was of interest to split the experience between the 29 distinct administrative areas within the County, each with different social characteristics, in order to seek some explanation of the differing local attack rates. An attempt was made to relate incidence to social and economic conditions generally, but no significant association was observed. The problem was then considered in terms of immunity. The association of high incidence in 1947 with low incidence in the previous ten years was tested, but no significant relationship was found. Similarly an attempt was made to relate the attack rate to the degree of dispersal of the population during the war—again without success. Then, bearing in mind the current theory that large outbreaks of poliomyelitis in the more hygienically advanced countries might be due to the absence of immunizing doses of infection in infancy such as are experienced in more backward countries, a theory supported by the steady fall in the proportion of cases under 5 from 55% in 1921 to 28% in 1947, they had tested one factor which might be connected with the general level of sanitation, namely housing conditions. They found, using up-to-date information of overcrowding, a significant negative correlation coefficient of  $-0.48$  between the poliomyelitis attack rate and the average number of persons per room in each administrative area, i.e. where more people were crowded together in the household, there was less overt poliomyelitis.

Periods between notification of those instances where more than one case occurred in the same family were recorded, and so many of them were less than three days that some point was given to the opinion of Dr. Percy Stocks (1932, *J. Hyg. Camb.*, 32, 219) that in these instances there was a single invasion of the family rather than case-to-case transmission within the family. Dr. Ian Taylor had called his attention to the comparative smoothness of the epidemic curve, despite the relatively small number of cases involved, and a mathematical examination of this problem suggested that the number actually exposed to risk was smaller and the attack-rate higher than might be supposed from mere examination of the number of notified cases, and suggested that poliomyelitis is an endemic disease of a subliminal nature, becoming epidemic when the level of immunity had fallen below a certain threshold value or when the virus had perhaps been transmuted to a more invasive type. How many subliminal attacks were there for every overt case notified? In 1932 Stocks (*loc cit.*), making use of the relationship between instances where only single cases in a family were notified and instances where more than one case in the family was notified, estimated the ratio to be 100 to 1 under endemic conditions. The speaker, using a somewhat similar method, had estimated the ratio to be 100 to 1 for the epidemic conditions of 1947, with probably a much higher ratio under endemic conditions.

**Dr. W. P. Sweetnam:** This meeting to-day reminds me vividly of just over twelve months ago; at that time I was working in the Public Health Department of Eccles Borough, where we were being continually asked by practitioners and the general public for advice on preventive measures. I wonder if there can be any other situation in which an M.O.H. feels so helpless.

I should like to bring to your notice some of the more instructive features of the Eccles outbreak (Sweetnam, W. P., 1948, *Brit. med. J.* (i), 1172). (1) The geographical spread of infection was confined to the western half of the borough for six weeks by a canal less than 25 feet wide. The fact that communications between the two halves of the Borough are restricted to two bridges over this canal, together with other epidemiological evidence, indicated that human contact played the major role in the spread of infection. There was only one instance of a paralytic case-to-case contact and it appeared that healthy carriers and abortive cases were mainly responsible for the spread of paralytic infections.

(2) A survey, undertaken in two areas of the Borough, revealed the widespread prevalence of abortive cases, especially in the immediate neighbourhood of frank cases. The figures obtained suggested a proportion of 15 abortive cases to 1 frank case.

(3) In this outbreak the nasopharynx rather than the intestine appeared the most important source of the virus.

Finally, I should be glad if anyone could offer an explanation of why, in the Eccles outbreak, 27 of the 46 total cases occurred in the 0-4 age group compared to only 31% of cases in this age group in the Country as a whole.

## Section of Otology

President—R. SCOTT STEVENSON, F.R.C.S.Ed.

[November 5, 1948]

### The Otologist and Rehabilitation of the Deaf

#### PRESIDENT'S ADDRESS

By R. SCOTT STEVENSON, F.R.C.S.Ed.

#### I

REHABILITATION has been defined as a planned method of treatment designed to use all the resources of the patient to bring about his complete adjustment to social and economic needs. It is a term which is already being used with a variety of meanings and is not to be confused with vocational training, which means training in new work a man incapacitated for his old work. Rehabilitation is concerned with both physical and psychological aspects. No cure is perfect which does not pay due regard to the restoration of function as well as to the control of infection or the removal of disease.

Rehabilitation of a case of deafness may include such measures as operations on tonsils, adenoids, or nasal sinuses; irradiation of the lymphoid tissue in the post-nasal space; or the fenestration operation for otosclerosis. I shall confine myself here to the consideration of the rehabilitation of cases of deafness for which such measures are of no avail, but which may be helped by means of a hearing-aid, lip-reading and auditory training.

In our specialty there have always been some members who have interested themselves particularly in the well-being of the deaf, whose disability we have been unable to cure. The founder in 1900 of the Otological Society which became this Section, Sir William Dalby, was one, and two former presidents, Dr. Kerr Love of Glasgow and Mr. Alexander Tweedie of Nottingham, were among others.

#### II

After the war of 1914-18, pensions were paid in this country for aural disabilities to 33,000 deafened ex-Service men, but there are only some 6,000 deafened pensioners from the war of 1939-1945. In the United States it was estimated that there would be a quarter of a million aural casualties from the last war—fortunately a gross over-estimate—and the first hearing centre was set up by the Army at the Walter Reed Hospital, Washington, D.C., early in 1943, and eventually there were three Army aural rehabilitation centres. The American Navy followed by establishing a similar centre at the Philadelphia Naval Hospital under Francis L. Lederer. Norton Canfield has done much, in association with E. P. Fowler, junr., Aram Glorig, and other otologists, for auditory rehabilitation, especially among ex-Service men, in the United States. Before the war there had been no such rehabilitation centres for deafened civilians, but this is less surprising when it is remembered that in Norton Canfield's film (1945, *Proc. R. Soc. Med.*, 38, 628) the scheme of training shown there occupied from five to eight weeks, during which time the deafened soldiers were kept in hospital or in a convalescent unit.

In this country a small number of hearing-aid clinics had already been set up in hospitals before the last war. Their establishment had been stimulated by the National Institute for the Deaf, which has long taken a particular interest in hearing-aids and in preventing the exploitation of the deaf by unscrupulous dealers. In 1929 it drew up an approved list of dealers, who agreed to maintain certain minimum ethical standards and particularly to allow a reasonable home trial of a hearing-aid for a small fee, and not to publish extravagant and misleading advertisements.

My special interest in auditory rehabilitation arose in the following way. Our Hearing-Aid Clinic at the Metropolitan Ear, Nose and Throat Hospital, established in the spring of 1937, was re-organized in September 1945, when the hospital resumed its peacetime activities, and at the beginning of this year, when the Government—following the report of the Electro-Acoustics Committee of the Medical Research Committee—had announced its intention of providing a valve-amplifier hearing-aid for deaf persons, as part of the National Health Scheme, we began to get inquiries from different parts of the country regarding the establishment of a hearing-aid clinic. We therefore examined the statistics of our own hearing-aid clinic, and were somewhat shocked to find that, in spite of our enthusiastic and well-trained staff and the trouble taken over each patient—a total of one and a half to two hours was being spent on each—in 1946 50% and in 1947 33.3% of the hearing-aids prescribed were being returned within a week or two. On inquiry, I found this was no surprise to the commercial dealers in hearing-aids, who were accustomed to allow for a minimum of 50% of hearing-aids lent on

Although the geographical spread within London was not worth following, it was of interest to split the experience between the 29 distinct administrative areas within the County, each with different social characteristics, in order to seek some explanation of the differing local attack rates. An attempt was made to relate incidence to social and economic conditions generally, but no significant association was observed. The problem was then considered in terms of immunity. The association of high incidence in 1947 with low incidence in the previous ten years was tested, but no significant relationship was found. Similarly an attempt was made to relate the attack rate to the degree of dispersal of the population during the war—again without success. Then, bearing in mind the current theory that large outbreaks of poliomyelitis in the more hygienically advanced countries might be due to the absence of immunizing doses of infection in infancy such as are experienced in more backward countries, a theory supported by the steady fall in the proportion of cases under 5 from 55% in 1921 to 28% in 1947, they had tested one factor which might be connected with the general level of sanitation, namely housing conditions. They found, using up-to-date information of overcrowding, a significant negative correlation coefficient of  $-0.48$  between the poliomyelitis attack rate and the average number of persons per room in each administrative area, i.e. where more people were crowded together in the household, there was less overt poliomyelitis.

Periods between notification of those instances where more than one case occurred in the same family were recorded, and so many of them were less than three days that some point was given to the opinion of Dr. Percy Stocks (1932, *J. Hyg. Camb.*, 32, 219) that in these instances there was a single invasion of the family rather than case-to-case transmission within the family. Dr. Ian Taylor had called his attention to the comparative smoothness of the epidemic curve, despite the relatively small number of cases involved, and a mathematical examination of this problem suggested that the number actually exposed to risk was smaller and the attack-rate higher than might be supposed from mere examination of the number of notified cases, and suggested that poliomyelitis is an endemic disease of a subliminal nature, becoming epidemic when the level of immunity had fallen below a certain threshold value or when the virus had perhaps been transmuted to a more invasive type. How many subliminal attacks were there for every overt case notified? In 1932 Stocks (*loc cit.*), making use of the relationship between instances where only single cases in a family were notified and instances where more than one case in the family was notified, estimated the ratio to be 100 to 1 under endemic conditions. The speaker, using a somewhat similar method, had estimated the ratio to be 100 to 1 for the epidemic conditions of 1947, with probably a much higher ratio under endemic conditions.

**Dr. W. P. Sweetnam:** This meeting to-day reminds me vividly of just over twelve months ago; at that time I was working in the Public Health Department of Eccles Borough, where we were being continually asked by practitioners and the general public for advice on preventive measures. I wonder if there can be any other situation in which an M.O.H. feels so helpless.

I should like to bring to your notice some of the more instructive features of the Eccles outbreak (Sweetnam, W. P., 1948, *Brit. med. J.* (i), 1172). (1) The geographical spread of infection was confined to the western half of the borough for six weeks by a canal less than 25 feet wide. The fact that communications between the two halves of the Borough are restricted to two bridges over this canal, together with other epidemiological evidence, indicated that human contact played the major role in the spread of infection. There was only one instance of a paralytic case-to-case contact and it appeared that healthy carriers and abortive cases were mainly responsible for the spread of paralytic infections.

(2) A survey, undertaken in two areas of the Borough, revealed the widespread prevalence of abortive cases, especially in the immediate neighbourhood of frank cases. The figures obtained suggested a proportion of 15 abortive cases to 1 frank case.

(3) In this outbreak the nasopharynx rather than the intestine appeared the most important source of the virus.

Finally, I should be glad if anyone could offer an explanation of why, in the Eccles outbreak, 27 of the 46 total cases occurred in the 0-4 age group compared to only 31% of cases in this age group in the Country as a whole.

## Section of Otology

President—R. SCOTT STEVENSON, F.R.C.S.Ed.

[November 5, 1948]

### The Otologist and Rehabilitation of the Deaf

#### PRESIDENT'S ADDRESS

By R. SCOTT STEVENSON, F.R.C.S.Ed.

#### I

REHABILITATION has been defined as a planned method of treatment designed to use all the resources of the patient to bring about his complete adjustment to social and economic needs. It is a term which is already being used with a variety of meanings and is not to be confused with vocational training, which means training in new work a man incapacitated for his old work. Rehabilitation is concerned with both physical and psychological aspects. No cure is perfect which does not pay due regard to the restoration of function as well as to the control of infection or the removal of disease.

Rehabilitation of a case of deafness may include such measures as operations on tonsils, adenoids, or nasal sinuses; irradiation of the lymphoid tissue in the post-nasal space; or the fenestration operation for otosclerosis. I shall confine myself here to the consideration of the rehabilitation of cases of deafness for which such measures are of no avail, but which may be helped by means of a hearing-aid, lip-reading and auditory training.

In our specialty there have always been some members who have interested themselves particularly in the well-being of the deaf, whose disability we have been unable to cure. The founder in 1900 of the Otological Society which became this Section, Sir William Dalby, was one, and two former presidents, Dr. Kerr Love of Glasgow and Mr. Alexander Tweedie of Nottingham, were among others.

#### II

After the war of 1914-18, pensions were paid in this country for aural disabilities to 33,000 deafened ex-Service men, but there are only some 6,000 deafened pensioners from the war of 1939-1945. In the United States it was estimated that there would be a quarter of a million aural casualties from the last war—fortunately a gross over-estimate—and the first hearing centre was set up by the Army at the Walter Reed Hospital, Washington, D.C., early in 1943, and eventually there were three Army aural rehabilitation centres. The American Navy followed by establishing a similar centre at the Philadelphia Naval Hospital under Francis L. Lederer. Norton Canfield has done much, in association with E. P. Fowler, junr., Aram Glorig, and other otologists, for auditory rehabilitation, especially among ex-Service men, in the United States. Before the war there had been no such rehabilitation centres for deafened civilians, but this is less surprising when it is remembered that in Norton Canfield's film (1945, *Proc. R. Soc. Med.*, 38, 628) the scheme of training shown there occupied from five to eight weeks, during which time the deafened soldiers were kept in hospital or in a convalescent unit.

In this country a small number of hearing-aid clinics had already been set up in hospitals before the last war. Their establishment had been stimulated by the National Institute for the Deaf, which has long taken a particular interest in hearing-aids and in preventing the exploitation of the deaf by unscrupulous dealers. In 1929 it drew up an approved list of dealers, who agreed to maintain certain minimum ethical standards and particularly to allow a reasonable home trial of a hearing-aid for a small fee, and not to publish extravagant and misleading advertisements.

My special interest in auditory rehabilitation arose in the following way. Our Hearing-Aid Clinic at the Metropolitan Ear, Nose and Throat Hospital, established in the spring of 1937, was re-organized in September 1945, when the hospital resumed its peacetime activities, and at the beginning of this year, when the Government—following the report of the Electro-Acoustics Committee of the Medical Research Committee—had announced its intention of providing a valve-amplifier hearing-aid for deaf persons, as part of the National Health Scheme, we began to get inquiries from different parts of the country regarding the establishment of a hearing-aid clinic. We therefore examined the statistics of our own hearing-aid clinic, and were somewhat shocked to find that, in spite of our enthusiastic and well-trained staff and the trouble taken over each patient—a total of one and a half to two hours was being spent on each—in 1946 50% and in 1947 33.3% of the hearing-aids prescribed were being returned within a week or two. On inquiry, I found this was no surprise to the commercial dealers in hearing-aids, who were accustomed to allow for a minimum of 50% of hearing-aids lent on

trial to be returned. According to K. M. Day (1940), in America it was calculated that 75% of all hearing-aids purchased were eventually discarded—in 1946 alone, 225,000 hearing-aids were bought in the United States, and it is calculated that 800,000 hearing-aids had been sold in that country. I read, however, in an article by Eva A. Thompson (1946), chief acoustic technician at the U.S. naval aural rehabilitation centre, that of 2,216 naval patients fitted with hearing-aids and who had gone through the four to eight weeks' rehabilitation programme, at the end of twelve months 94% continued to wear their aids with satisfaction. The contrast with our own experience was so marked that I resolved to visit the United States and study the aural rehabilitation clinics there, to see whether their methods could be applied to ordinary civilian life—for it is obvious that the Services' training programme of residence in a hospital for several weeks was out of the question.

With the aid of a grant from the Ernest Latham Bequest to the Metropolitan Ear, Nose and Throat Hospital, I was able to visit the United States and study aural rehabilitation clinics. The Army has its auditory rehabilitation work now centred at Forest Glen, in Washington, D.C., and the Navy at the Naval Hospital, Philadelphia, while the Veterans Administration centre in the East is in New York; at all of these the staffing and the programme is much the same, differing in minor details only. At St. Louis, the Central Institute for the Deaf, founded in 1914 by that great pioneer of the welfare of the deaf, Dr. Max Goldstein, has under one roof a residential school for deaf-mute children and a training college for teachers of the deaf, a hearing-aid clinic (in association with the hospital ear, nose and throat department), and well-equipped neuro-otological, physical and psychological research laboratories; many of the methods and much of the equipment employed at the other auditory rehabilitation centres have been designed at the Central Institute. A particularly interesting clinic is that at the Illinois Eye and Ear Infirmary in Chicago, under the direction of Francis L. Lederer (1946), for there a modern well-equipped clinic has been set up in the basement of an 80-year old hospital. I also visited New Orleans and Cleveland, where there are organizations for the welfare of the deaf, but not clinics of the same type as the other centres.

### III

I returned greatly impressed with the value of what is termed "auditory training", in association with the careful testing of the hearing (always in sound-proof rooms), selection and provision of hearing-aids (always with an individual insert), and lip-reading or "speech-reading" classes. Their hearing-aids are no better than ours, but the equipment and the staffing of the centres are outstanding. It is noticeable that the leading figure at each centre is a psychologist, usually with a background of experience in teaching the deaf, and not an otologist. To my mind there is a potential danger in this, which has not gone unnoticed in America. Macfarlan (1948), observes that the enlightened deaf public is expecting better hearing testing work from the otologist; if we do not undertake the obligation, he says, we shall experience the advent of the half-trained lay technician or "audiologist", who will assume a rôle largely beyond his capacity.

At the New York Veterans Aural Rehabilitation Unit—which was planned by E. P. Fowler, junr., and cost 80,000 dollars in a building already there—there are 22 rooms, 4 of them sound-proofed; the staff consists of the administrator (who is an "audiologist" with an M.A. degree and a background of having taught the deaf), 4 clinical acoustic specialists, men or women, all M.A.s, 1 lip-reading and speech specialist (an M.A., who does the planning), 1 full-time psychologist (an M.A.), 3 lip-reading teachers, 2 speech-correctionists, and 2 auditory training teachers (all of these with university degrees), 2 technicians (who construct and maintain the electro-acoustic equipment), 1 hearing-aid repair man (formerly a radio expert—he wears a hearing-aid), and 4 clerks. The medical consultants comprise 3 half-time otologists and one half-time psychiatrist.

At Lederer's unit in Chicago the staff is 1 full-time otologist, 1 director of education (Ph.D.), 1 teacher of the young deaf (Ph.D.), 1 full-time audiometrist (B.A.), 1 full-time electronics engineer (B.A.), 1 hearing-aid technician (B.A.), 1 full-time speech therapist—besides one full-time teacher of laryngectomized speech, not concerned with this problem. In the Philadelphia Naval Hospital the staff is now a mere skeleton compared with what it was during the war, though it maintains its efficiency and its enthusiasm. A detailed account of the auditory training in New York will cover the work done at the other centres.

### IV

At the New York Veterans Aural Rehabilitation Unit the work of the two auditory training teachers is the adjustment of the veteran to the hearing-aid; they also attend to the veterans' complaints and try to find out what the problem is; they are "hearing-aid counsellors" in addition to their teaching duties. All veterans are referred by an ear, nose and throat surgeon, in order to screen disease. When they come to the unit they have an audiogram and a spoken voice test—the last admittedly inaccurate but done because of

the pension which is still based on this: the percentage is based on the hearing of the two ears. Then they go to the unit otologist, who decides whether the deafness is static or progressive, that radium in the post-nasal space will not help it, that the fenestration operation is not indicated, and that rehabilitation is necessary. Next the veteran is seen by an "interviewer", whose job is to persuade him to come for a four weeks' programme; the interviewer also makes arrangements with the veteran's employer. When a hearing-aid is indicated, at this stage the veteran is sent to have an impression for an ear insert—all veterans use individual ear-moulds. The veteran usually begins his course in the following week, starting on a Monday—one group starts in the morning, the next group starts in the afternoon. When there is any doubt about a psychogenic factor the veteran is seen by a social worker, though this is not routine, who presents his results to the psychiatrist. A diagnostic study is then made and psychotherapy is given if necessary. The psychiatrist may or may not enter the patient for rehabilitation.

The veteran comes to see the interviewer with his folder, which contains his audiogram, air and bone conduction readings, and controlled speech tests (it is the distance that is controlled, spondee word lists used, unilaterally, with the other ear masked by about 75 decibels "white noise"); also the otologist's findings and recommendations. A "case record" of basic information is made out—whether or not he has ever worn a hearing-aid or learned lip-reading, also information about his occupation and what practical difficulties he is having. He is reassured about the difficulties of a hearing-aid, persuaded of its value, and instructed in its mechanics and its upkeep.

The following is the programme: (1) Audiogram, otological examination, preliminary interview. (2) Auditory training, including training in the use and care of the aid. (3) Lip-reading. (4) Speech correction and voice control. (5) "Orientation" lectures. The training consists of four weeks, five half-days a week, 8.30 to 12 noon, or 1 to 4.30; four forty-five minute periods, with a ten minutes' break between each. How can the veteran arrange his own work-programme for this? His employer may readjust his working hours. He may come during his vacation, or may take his vacation in advance. Some see that they need the programme so much that they take leave from their job with or without pay. Some may have even to give up their job in order to take the programme, and the veterans social welfare officer has to find another job for them afterwards. Some men have reluctantly to give up any idea of the programme for financial reasons—and it is for them that a three-day compressed intensive programme was designed, but this only gives a sample of the information and cannot be a complete scheme of rehabilitation.

Auditory training consists in foreseeing the auditory problems and showing the man what he can hear in a given situation. Noise background discs are played on the gramophone and the patient is spoken to over this—at first the noise is quiet and then increased, so that eventually the noise is louder than the conversation. Every hearing-aid picks up all sounds and amplifies them to the same degree; the man must therefore be trained to use his hearing-aid in a noise—and this can be done.

Listening exercises start with a simple song, such as Bing Crosby singing to a piano accompaniment, then on to some more elaborate song, a duet or trio, and then on to orchestras; often in the album of records from a musical show there will be useful gradations of difficulty. Then the men go on to quite difficult recordings, such as an opera singer with a foreign accent, and then on to very rapid singing or speech, such as a long complicated song from "Finian's Rainbow"—the man has the script in front of him, but later they use scripts with some words missed out. The man has to learn the range of his hearing-aid—with a steel measure the distance from the man is measured (e.g. accurately at 6 feet, or at 18 feet), and he is shown this. Attention and inattention are studied and explained—the hard-of-hearing are often inattentive. The problem of deaf people withdrawing from society is studied with the men—they must drive themselves to get back again. The men are given telephone practice—ordinary telephone booths are used—to teach them how to use the every-day telephone. One day is devoted to a general discussion of audiograms—at the end of the second week. High-frequency loss curves and low-frequency loss curves are plotted, and the next day the exact audiograms of all the men in the group are plotted and compared—this has a very salutary effect. Such practical suggestions are made as where to sit in the cinema and where not to sit—moving one seat away may make a tremendous difference; the men are advised to study the acoustic problems of different rooms. Any noise will distract unless one knows its source (e.g. a refrigerator).

The veterans are told that some degree of hearing loss is very common, but information upon it is scarce. The man is not going to wear a hearing-aid for his own convenience alone, but for the sake of other people as well. The hearing-aid should be put on, adjusted as well as possible and then left alone—it is then the other person's problem and not his. In the first week of the course all the men are fidgeting with their hearing-aids, the second a little, the third they should not, and the fourth they do not do it. They must be persuaded to leave the hearing-aid alone. It is not possible to localize with a hearing-aid; sounds that

sound alike (e.g. T and K, S and F) look different in lip-reading; and sounds that look alike in lip-reading (e.g. P, D and M) sound very different. That is why a lip-reading background is necessary and the two have to be put together. "A hearing-aid and lip-reading are opposite sides of the same coin", as I was told at the New York Unit.

## V

Every veteran who comes into the programme is examined to determine whether he needs speech training and voice control. The quality or the pitch of the voice may be affected. Frequently there are anomalies in articulation, in the sibilant group especially. The meningitis cases with 100% hearing loss often have complete chaos in quality—the auditory image control is gone. About 75% of the men who come into the programme require some degree of speech training or voice control; about 30% (especially old nerve deafness cases) have serious speech problems. A recording of the voice is made, analysed and explained. Then training is begun, a decibel meter being used for volume control. The man is trained to project his voice, or to reduce it if it is too loud. It takes much co-operation by the man, as the time available is short. Speech should be audible, intelligible and reasonably pleasant. Five lectures on speech conservation are given, in which a man's present speech level is maintained. Men who have been trained are asked to come for a check-up twice a year.

One hour of each of the four hours in the first two weeks is devoted to lip-reading. In the third and fourth weeks they have in addition more advanced sight-reading, such as looking at little one act plays played by the staff. Altogether thirty hours of lip-reading are given in the four weeks' course. The men wear their hearing-aids in the lip-reading classes. The lip-reading teachers use a compromise of the Nitchie and Jena (speech-reading) systems, and they use the Jena charts. A veteran is tested on the Monday of his first week and the same test is given on the Friday of the first week. On the last day of the course, he gets a proficiency test and is graded below-average, average, or above-average. It is found that a concentrated day-after-day course is much better than lessons given once a week for several weeks. The veteran's wife, or some other member of his family, is invited in the third week for a sample lesson, in order to help at home with the lip-reading.

## VI

Auditory training improves understanding by helping the methods of communication. It is not a treatment of deafness and the deafness itself is not affected. At the auditory rehabilitation centres the different departments are by no means watertight compartments, but overlap each other. The work must obviously be done by well-trained technicians, but it does seem to me that it should be co-ordinated directly under the supervision of an otologist, rather than by using the otologist as a consultant.

What proof is there that auditory training is worth while? S. R. Silverman (1944) has described how seven users of hearing-aids were given auditory training twice a week for ten weeks. Since wearers of hearing-aids should adjust to normal patterns of social communication, no attempt was made to keep the room quiet, but windows were kept open purposely to allow the noise of heavy traffic and of voices in the corridor to be heard. Six of the seven patients showed improvement in the understanding of speech as a result of the training—the other case was a patient who began with no appreciation of speech through a hearing-aid. Understanding of words improved from zero to 36% and of sentences from 8 to 52%. Dr. and Mrs. Ewing (1947) in this country and C. V. Hudgins (1948) in America have shown convincingly that a hearing-aid *plus* lip-reading is infinitely better than a hearing-aid alone.

But the most evident proof is the very much smaller percentage of hearing-aids returned by those deaf persons who have undergone training, compared with those who have not done so. At the Hoff Military Hospital, before they began to use auditory training, a large number of the deafened veterans were dismissed as quite unable to make any use of a hearing-aid; but after the introduction of auditory training and lip-reading, every man was able to benefit from using a hearing-aid. At the Naval Hospital, Philadelphia, 2,216 patients were fitted with hearing-aids (only 65 of the bone-conduction type), and 6 men only were unable to benefit from the use of a hearing-aid, a course of auditory training being given in every case.

## REFERENCES

- DAY, K. M. (1940) *Penn. med. J.*, **43**, 1299.  
 EWING, A. W. G. (1947) *Practitioner*, **158**, 129.  
 HUDGINS, C. V., quoted by BERRY, G. (1948) *Ann. Otol. Rhin. Laryng.*, **57**, 500.  
 LEDERER, F. L., and HARDY, W. G. (1946) *Arch. Otolaryng.*, *Chicago*, **43**, 429.  
 MACFARLAN, D. (1948) *Ann. Otol. Rhin. Laryng.*, **57**, 444.  
 SILVERMAN, S. R. (1944) *Laryngoscope*, *St. Louis*, **54**, 29.  
 THOMPSON, EVA A. (1946) *Nav. Med. Bull.*, *Wash. Suppl.* March, 216.

# PROCEEDINGS *of the* ROYAL SOCIETY OF MEDICINE

ISSUED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE:

HONORARY EDITORS

ERIC A. CROOK      E. R. CULLINAN

EDITOR

J. M. BROWNE KUTSCHBACH

|                                           |                                 |
|-------------------------------------------|---------------------------------|
| G. S. W. ORGANE (Anæsthetics)             | F. T. RIDLEY (Ophthalmology)    |
| J. S. RICHARDSON (Clinical)               | H. L.-C. WOOD (Orthopædics)     |
| J. B. BROOKSBY (Comparative Medicine)     | C. S. HALLPIKE (Otology)        |
| E. W. PROSSER THOMAS (Dermatology)        | A. G. SIGNY (Pædiatrics)        |
| E. F. SCOWEN (Endocrinology)              | F. R. SELBIE (Pathology)        |
| ALLAN McFARLAN (Epidem. & State Med.)     | M. B. RAY (Physical Medicine)   |
| A. C. WHITE (Exper. Med. & Therap.)       | O. V. LLOYD-DAVIES (Proctology) |
| I. E. McCracken (History of Medicine)     | DENIS HILL (Psychiatry)         |
| W. A. MILL (Laryngology)                  | F. CAMPBELL GOLDING (Radiology) |
| MAURICE DAVIDSON (Medicine)               | CHARLES DONALD (Surgery)        |
| J. St. C. ELKINGTON (Neurology)           | G. M. FINDLAY (United Services) |
| LESLIE WILLIAMS (Obstetrics & Gynæcology) | A. CLIFFORD MORSON (Urology)    |
| B. W. FICKLING (Odontology)               |                                 |

SECRETARY OF THE ROYAL SOCIETY OF MEDICINE

G. R. EDWARDS





## REDUCTION IN STRENGTH

**ETHIN-OESTRYL**  
Ethinyl-Oestradiol (Roussel)

THE MOST POTENT ORAL OESTROGEN

## NEW PRESENTATION

### 10 gamma tablets (0.01 mgm.)

The new 10 gamma tablets are SUFFICIENT for the majority of gynaecological cases. They should be used in preference to 50 gamma tablets reserved for special treatments requiring high doses, e.g. Prostatic Carcinoma.

*0.01 mgm. tablets and 0.05 mgm. tablets  
Bottles of 25, 100, and 500.*

SAMPLES ON REQUEST



ROUSSEL LABORATORIES LIMITED  
Distributors: Antigen Laboratories Ltd.  
95 Great Portland St., London, W.1. LAN. 3744

# PROCEEDINGS

## OF THE

# ROYAL SOCIETY OF MEDICINE

Vol. XLII    No. 2    February 1949

## CONTENTS

Whole  
Proceedings  
Page

### Section of Obstetrics and Gynaecology

|                                                                                                                 |    |
|-----------------------------------------------------------------------------------------------------------------|----|
| Central Placenta Praevia.—V. B. GREEN-ARMYTAGE, F.R.C.O.G. . . . .                                              | 59 |
| Endometriosis of the Bladder: Tumour Arising in Wolffian Remnants.—J. B. BLAIKLEY, F.R.C.S., F.R.C.O.G. . . . . | 59 |
| Adenofibroma of Ovary with Partial Differentiation to Endometriosis.—P. E. HUGHESDON, M.B. . . . .              | 62 |
| Pre-Invasive Cancer of the Cervix (Bowen's Disease). Report on Two Cases.—ROSA HERTZ, M.B. . . . .              | 63 |
| Extramembranous Pregnancy.—MARY K. LAWLOR, F.R.C.S.Ed., M.R.C.O.G. . . . .                                      | 64 |

### Section of Neurology

. MEETING HELD AT THE NATIONAL HOSPITAL, QUEEN SQUARE, LONDON

|                                                                                                                                                                                     |    |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----|
| Persistent Rhythmic Contractions of the Ipsilateral Pharynx, Larynx, Vocal Cord, Face and Arm Following Trauma.—G. MILTON SHY, M.R.C.P., and E. ARNOLD CARMICHAEL, F.R.C.P. . . . . | 65 |
| (1) Familial Myoclonus and Congenital Morbus Cordis . . . . .                                                                                                                       | 66 |
| (2) Abnormal Ocular Movement . . . . .                                                                                                                                              | 66 |
| FRANK A. ELLIOTT, F.R.C.P.                                                                                                                                                          |    |
| (1) ? Manganese Intoxication . . . . .                                                                                                                                              | 66 |
| (2) ? Peduncular Hallucinosi . . . . .                                                                                                                                              | 67 |
| MACDONALD CRITCHLEY, M.D., F.R.C.P.                                                                                                                                                 |    |
| Generalized Neurofibromatosis with Intracranial Mass and Pulsating Enophthalmos.—R. E. KELLY, M.D., M.R.C.P. (for S. P. MEADOWS, M.D., F.R.C.P.) . . . . .                          | 67 |
| (1) Facial Palsy, Bilateral . . . . .                                                                                                                                               | 68 |
| (2) Blindness, Ophthalmoplegia and Sensory Polyneuritis . . . . .                                                                                                                   | 68 |
| DENIS WILLIAMS, M.D.                                                                                                                                                                |    |

### Section of Laryngology

|                                                                                                                              |    |
|------------------------------------------------------------------------------------------------------------------------------|----|
| The Last Ten Years—Some Experiences and Reflections. [ <i>Abridged</i> ].—President's Address by E. COWPER TAMPLIN . . . . . | 71 |
|------------------------------------------------------------------------------------------------------------------------------|----|

### Section of Pædiatrics

|                                                                                                                                                                                               |    |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----|
| Partial Hemihypertrophy Affecting Right Leg.—J. R. D. WEBB, O.B.E., M.R.C.P., D.P.H., D.C.H. . . . .                                                                                          | 77 |
| Albers-Schönberg Disease.—S. B. DIMSON, M.D., M.R.C.P. . . . .                                                                                                                                | 77 |
| Osteogenesis Imperfecta Presenting With Delay in Walking (Two Cases).—J. P. M. TIZARD, M.R.C.P. (for W. G. WYLLIE, M.D., F.R.C.P., and BERNARD SCHLESINGER, O.B.E., M.D., F.R.C.P.) . . . . . | 80 |
| Acute Infective Polyneuritis.—HUGH R. JOLLY, M.R.C.P. (for WILFRID SHELDON, M.D., F.R.C.P.) . . . . .                                                                                         | 83 |
| Hepatic Glycogen Disease.—L. G. SCOTT, M.B. (for P. R. EVANS, M.D., F.R.C.P.) . . . . .                                                                                                       | 84 |
| Sarcoidosis.—MEGAN P. JONES, M.B., D.C.H. (for URSULA JAMES, M.R.C.P.) . . . . .                                                                                                              | 85 |
| Fersolate Poisoning.—R. C. ROXBURGH, M.B. (for CHARLES F. HARRIS, M.D., F.R.C.P.) . . . . .                                                                                                   | 85 |
| Calcified Intrathoracic Tumour in an Infant. ? Dermoid Cyst.—J. DEAN, M.R.C.P. (for IAN M. ANDERSON, M.D.) . . . . .                                                                          | 86 |
| Xanthomatosis.—P. M. SMYTHE, M.R.C.P. (for R. H. DOBBS, M.D., F.R.C.P.) . . . . .                                                                                                             | 86 |

(Continued on next page)

## Section of Pædiatrics~(continued)

|                                                                                                                                     |    |
|-------------------------------------------------------------------------------------------------------------------------------------|----|
| Pulmonary Hæmosiderosis.—ALISON B. KING, M.B. (for MARY WILMERS, M.D.) ..                                                           | 87 |
| Multiple Aneurysms (? Congenital).—D. A. J. WILLIAMSON, M.D., M.R.C.P. (for<br>BERNARD SCHLESINGER, O.B.E., M.D., F.R.C.P.) .. .. . | 87 |

## Section of Orthopædics

|                                                                                                                            |    |
|----------------------------------------------------------------------------------------------------------------------------|----|
| Infective Arthritis of the Left Hip-Joint.—W. E. TUCKER, F.R.C.S. .. .. .                                                  | 89 |
| Tuberculous Disease of the Spine Simulating Malignancy in a Male Patient aged 30.—<br>P. I. HYWEL-DAVIES, F.R.C.S. .. .. . | 90 |
| I. End-results of Amputation of Great Toe and First Metatarsal .. .. .                                                     | 91 |
| II. Charcot's Disease of the Hip-Joint .. .. .                                                                             | 91 |
| III. Symmetrical Talipes Equino-Varus in Identical Twins .. .. .                                                           | 93 |
| R. C. F. CATTERALL, F.R.C.S.                                                                                               |    |
| I. Polyostotic Fibrous Dysplasia .. .. .                                                                                   | 94 |
| II. Generalized Osteopetrosis .. .. .                                                                                      | 95 |
| G. P. ARDEN, F.R.C.S.                                                                                                      |    |
| Bilateral Compound Palmar Ganglia.—ROSS BLOOM, F.R.C.S. .. .. .                                                            | 96 |
| Charcot's Disease Affecting Both Knees and One Hip.—J. S. BATCHELOR, F.R.C.S. ..                                           | 98 |
| Elephantiasis Nervorum.—P. MARCHAND, M.B. (introduced by K. I. NISSEN, F.R.C.S.)                                           | 98 |

## Section of Anæsthetics

|                                                                                                                                                         |    |
|---------------------------------------------------------------------------------------------------------------------------------------------------------|----|
| Recent Impressions of Anæsthesia in the United States of America and in Canada.—<br>President's Address by RONALD JARMAN, D.S.C., F.F.A. R.C.S. .. .. . | 99 |
|---------------------------------------------------------------------------------------------------------------------------------------------------------|----|

## Clinical Section

October 8, 1948

|                                                                                            |     |
|--------------------------------------------------------------------------------------------|-----|
| Subpleural Fibroma with Hypertrophic Osteo-Arthropathy.—LEO RAU, M.D.,<br>M.R.C.P. .. .. . | 103 |
| Rodent Ulcer of Anus.—GERALDINE BARRY, M.S., F.R.C.S. .. .. .                              | 104 |

November 12, 1948

|                                                                                                                                                               |     |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|
| Idiopathic Ulcerative Colitis with Severe Ulceration of the Skin and Peritonitis.—<br>A. G. LEISHMAN, M.B., M.R.C.P. (for B. BARLING, M.D., F.R.C.P.) .. .. . | 105 |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|

## Section of the History of Medicine

|                                                                       |     |
|-----------------------------------------------------------------------|-----|
| Sir William Knighton, Bart., 1776-1836.—HARLEY WILLIAMS, M.D. .. .. . | 107 |
|-----------------------------------------------------------------------|-----|

(N.B.—The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.)

Copyright: The Society holds the copyright of all matter accepted for publication in the *Proceedings*. Requests for subsequent publication elsewhere should be made to the Honorary Editors. All papers, &c., presented at meetings (other than those which have been previously published) are held to be subject to the Society's copyright until a decision in regard to their publication has been made.

Digests: Requests for permission to make Digests from the *Proceedings* should be addressed to the Honorary Editors.

All communications concerning Editorial Business should be addressed to  
THE HONORARY EDITORS, 1, WIMPOLE STREET, LONDON, W.1

Applications for advertisement space in the "*Proceedings*" should be made to the Society's official advertising agents, Messrs. C. Mitchell & Co. Ltd., Mitchell House, 1 and 2, Snow Hill, London, E.C.1.

Copies of the whole *Proceedings* may be purchased through any bookseller. Prices are as follows:—

|                                                                     |                           |
|---------------------------------------------------------------------|---------------------------|
| Single copies .. .. .                                               | 10s. 6d. each, post free. |
| Annual subscription, covering 12 monthly issues and annual index .. | £6 6s. 0d.                |

Reprints of Sectional parts may be obtained direct from the Society. Prices are as follows:—

|                             |                          |
|-----------------------------|--------------------------|
| Single copies .. .. .       | 3s. 6d. each, post free. |
| Annual subscription .. .. . | 15s. 0d.                 |

Fellows and Members of the Royal Society of Medicine are asked to apply direct to the Society for any copies of the *Proceedings* they may require, whether whole or Sectional, in addition to those they receive *gratis*. Prices are as follows:—

|                                                              |                          |
|--------------------------------------------------------------|--------------------------|
| Whole <i>Proceedings</i> :                                   |                          |
| Single copies .. .. .                                        | 7s. 6d. each, post free. |
| Complete volume (12 monthly issues and annual index) .. .. . | £5 0s. 0d.               |

|                                |                          |
|--------------------------------|--------------------------|
| Sectional <i>Proceedings</i> : |                          |
| Single copies .. .. .          | 3s. 0d. each, post free. |
| Annual subscription .. .. .    | 10s. 0d.                 |

## Section of Obstetrics and Gynæcology

President—Professor HILDA N. LLOYD, F.R.C.S., F.R.C.O.G.

[November 19, 1948]

**Central Placenta Prævia.**—V. B. GREEN-ARMYTAGE, F.R.C.O.G.

Mrs. B., aged 24, primipara.

16.4.47: She had arrived in hospital almost pulseless a few hours previously with a history of a severe flooding. She was 30 weeks pregnant. No fetal heart sounds or movements could be heard. The urine was clear and the abdomen soft. Two pints of blood were transfused and a fundal Caesarean performed—the foetus being removed in its complete sack with the placenta, prævia and central, type 4.

My reasons for showing this specimen are three:

First, that this condition of central placenta prævia with colossal hæmorrhage before the 34th week is not uncommonly seen and may demand emergency surgery. It is well known that then the lower segment from a surgical point of view hardly exists, and therefore incision through it infers tearing through a thick wall, leading to much trauma, hæmorrhage and shock.

Secondly, that the classical incision very often means disaster, for such an incision sets up the reflex of polarity—that is, as the uterus contracts, the lower segment dilates. There can be few obstetricians of experience who have not seen a tremendous output of blood into the vagina, sometimes leading to death on the table, a state of affairs which is preventable if, instead of the classical incision, the uterus is eventrated and an antero-posterior incision made at the top of the uterus in that groove which is always to be seen denoting the line of fusion of the primitive müllerian tracts. This line of incision at the top of the uterus is almost bloodless and permits the surgeon to slip his hand between the membranes and the uterine wall right down to the cervix, enabling the whole sack to be removed intact with practically no loss of blood. If the baby is alive the sack is handed to an assistant who breaks it and the baby cries. If need be the anæsthetist gives the mother an injection of ergometrine intravenously.

The third reason in favour of the fundal incision is that it is of particular value to those obstetricians who may be called to operate upon anæmic and badly nourished patients in the tropics who cannot stand the loss of any serious quantity of blood.

I speak from great experience of this operation and would particularly commend it to younger members of this Section who may be confronted with a case of central placenta prævia early in their career.

If the incision is sewn with nylon or silkworm gut there is no risk of secondary rupture, and provided that the omentum is put well behind the uterus before closing the abdomen, there is no likelihood of intestinal obstruction or ileus. This particular patient was confined of a healthy 8-lb. baby seventeen months after the operation described above.

**Endometriosis of the Bladder: Tumour Arising in Wolffian Remnants.**—J. B. BLAICKLEY, F.R.C.S., F.R.C.O.G.

This tumour was probably not a true endometrioma of the bladder but arose in vestigial remnants of the wolffian duct. The symptoms were typical of endometriosis vesicæ, but endometriosis must surely develop after the onset of menstruation, and not beforehand as in this case. Selye [1] says: "No definitely identified case of prepubertal endometriosis was found in a survey of the entire world literature; a few cases have been reported between 16 and 20 years."

Mrs. P. B., aged 28, was referred to me for severe dysmenorrhœa and dysuria. The first occasion on which she had the pain of which she complained, was on Christmas Eve 1929, when she was 10 years old. She then had a "violent stomach

ache" which lasted several days. There was no difficulty of micturition. A month later she saw her first period and suffered pain on the first day, and she had had considerable pain with every period since. Originally, this was situated more or less in the mid-line, but as she got older it was mostly low down in the left iliac fossa. It tended to get worse and last longer. The menses were always regular every twenty-eight days, lasting five.

She first noticed difficulty with micturition ten years ago, there was pain at the beginning and end of the act, but only during menstruation. For the last two years she stated she had had frequency between the periods, every fifteen minutes during the day and twice at night, and during a period there was, in addition, difficulty of micturition. She married two years ago and there had always been dyspareunia. The day after intercourse there was pain in the lower abdomen and in the lower back.

She has one child, born on February 5, 1948. During the pregnancy there was no pain and no difficulty of micturition. She had a period six weeks after delivery



FIG. 1.  $\times 24$



FIG. 2.  $\times 233$

Photomicrographs of tumour showing gland spaces. Fig. 2 shows low columnar epithelium and absence of true stroma.

when the pain was worse than ever before, and she experienced complete retention of urine for the first twelve hours. In April, May, and June, the pain continued to be very severe and she continued to have retention during the first twelve hours of menstruation and much frequency at other times.

When I examined her in July, I could feel a tender swelling through the left fornix. Under an anæsthetic a few days later this was felt to be the size of a walnut and appeared to be in the left broad ligament. I diagnosed an endometrioma involving the bladder and proceeded to open the abdomen. I then found she had also a small tumour, the size of a cherry, protruding into the broad ligament from the left side of the fundus, just below the round ligament. I removed this with some slight difficulty as it was not encapsulated. The tumour in the broad ligament I exposed by dividing the left round ligament and incising the adjacent anterior layer of the broad ligament. It was not attached to peritoneum. The tumour was adherent to the left side of the cervix and obviously involved the bladder wall deeply. The left ureter could be demonstrated running into the lateral aspect of it. The exposure was good, and it was easy to ligate the uterine vessels and then to dissect the ureter out of the tumour, which I next freed from the cervix, using scissors. It only remained to excise the mass from the bladder in which it was deeply embedded. It became evident that the vesical mucous membrane was adherent and, therefore, a small

portion was removed along with the tumour; the bladder was sutured, the peritoneum closed and a rubber drain placed down to the site of the suturing. She was put back to bed with an indwelling catheter.

Apart from a very temporary urinary leak a few days later, she made an uneventful recovery, and she has written to me recently to say that she has been entirely free from pain and from any dysuria in the three months since the operation.

The tumour had no capsule and in general structure resembled an endometrioma in that it was friable, had that granular feel that is so characteristic, and obviously contained a number of small cysts. They, however, contained mucus and no blood. The sections (figs. 1 and 2) show the cystic spaces to be lined by a low columnar epithelium, but there is no true stroma whatever and although endometriomata vary in this respect, I would suggest that this is one reason for supposing this tumour is not in fact an endometrioma. I had hoped that the small tumour attached to the fundus would be informative, but on section it has the normal structure of the myometrium and no epithelium can be found. It occurred to me that these two tumours, being both to the left of the uterus, might well have taken origin in remnants of the wolffian duct. I shortly afterwards read Huffman's article, with a review of the literature, on "Mesonephric Remnants in the Cervix" [2]. He does not, I find, describe any instance in which these remnants gave rise to tumours outside the cervix, and only found them in its substance. He says remnants occur in only 1% of cervixes, but quotes Robert Meyer as having found vestigial remains in as many as 20%, but the possibility does, I think, remain.

I am told by Professor T. B. Johnston and Professor Willis of the Department of Anatomy, Guy's Hospital, that 75% of anatomists would agree that wolffian duct remnants can occur in the situation of this tumour. Apart from the appearance of the sections, in particular the absence of any true stroma, I would again suggest that the early onset of quite severe dysmenorrhœa at the age of 10 suggests that the tumour was then already present, and that this strongly supports my contention that it arises in vestigial remains of the wolffian duct.

The absence of any connexion with peritoneum excludes serosal metaplasia or retrograde spill as the origin of this tumour. It seems to me quite likely that structures derived from the wolffian duct would react to œstrogens, but I may be wrong; Professor Zuckerman, in a personal communication, tells me that whereas amphibia certainly produce œstrogens, there is no evidence in favour of my supposition. It would seem likely that in other cases tumours in this situation have developed at a later age and their origin is therefore more open to doubt. I have myself no difficulty in believing that "endometriosis" arises in different ways and while such tumours as this are, I think, to be explained by von Recklinghausen's embryonal theory, Robert Meyer's theory of serosal metaplasia and Sampson's theory of retrograde spill explain the more common varieties, as is generally recognized.

Moore, Herring and McCannel [3] reviewed 46 cases of endometriosis of the bladder reported up to 1943. In 21 a tumour was palpable, it was irregular, firm, and often tender. 40 of these patients complained of cyclic bladder disturbance from two to fourteen days in duration over the time of each period. Symptoms were of pressure, dysuria, and frequency; 13 had gross hæmaturia. Pain was very variable, and was in some quite slight, in others severe. Cystoscopy immediately before a period showed variable findings, but typically, an elevated area with the surrounding mucosa showing congestion and œdema could be seen, also small translucent cysts, in colour bluish or blue-black. Between periods there was less to see. The tumours were commonest in the region of the trigone. In only three was the ureter involved.

Müller has reported a patient who, like mine, was quite well during pregnancy,

but after an abortion had dysmenorrhœa of increased severity when normal menstrual function returned.

Richard B. Phillips [4], reviewing 29 cases of endometriosis vesicæ recorded up to 1934, states that: "The stroma may be cytogenic or fibrous; in true endometriosis it must be the former. If the tissue is examined during the menstrual period, the typical changes occurring in the uterus will be observed in the extra-uterine growth." He says there is always a round-cell inflammatory reaction in the tissues around the tumour. Apart from this I find little description of the histology of these tumours. My own sections show a fibrous stroma if there is any stroma at all. The epithelium is low columnar, and the secretion in the gland spaces stains with mucicarmine. It is to be noted that the menstrual cycle was twenty-eight days and operation was performed eight days before the expected onset of the next period.

#### REFERENCES

- 1 SELYE, H. (1946) *Encyclopaedia of Endocrinology*, Montreal, 7, Sec. IV.
- 2 HUFFMAN, J. W. (1948) *Amer. J. Obstet. Gynec.*, 56, 23.
- 3 MOORE, T. D., HERRING, A. L., and McCANNEL, D. (1943) *J. Urol.*, 49, 171.
- 4 PHILLIPS, R. B. (1934) *J. Obstet. Gynec. Brit. Emp.*, 41, 165.

#### Adenofibroma of Ovary with Partial Differentiation to Endometriosis.—P. E. HUGHESDON, M.B.

*History*.—Long and varied medical history, the principal items being pernicious anæmia with subacute combined degeneration (from 1943), hypertension 170/100 (from 1946), recurrent urinary tract infection (from 1945).

The patient was aged 53 at the time of operation; single, para-O, *virgo intacta*.

*Menstrual history*.—Puberty 1908. 2-3/35-42, always irregular and painful on first day. August 1945 became still more irregular, with development of hot flushes. August 1947 periods stopped. End of May 1948 she had a single loss lasting a week.

*On examination*.—In March 1947 she complained of backache. Examination under anæsthesia by Professor W. C. W. Nixon disclosed a mobile craggy mass in the left fornix, interpreted as a slightly enlarged left ovary. No action was taken. In June 1948, whilst under investigation for recurrent pyelitis, she was again seen by Professor Nixon and a hard craggy mass felt behind, to the left of and separate from the uterus. In view of recent developments operation was advised.

*At operation* on 16.7.48, the specimen was removed; a few ounces of blood-stained fluid were found in the pouch of Douglas, but no adhesions or other signs of a fully developed endometriosis.

*Pathology*.—Both ovaries are enlarged (R.  $\times 2$ , L.  $\times 4$ ) by solid, nodular, growths whose surfaces are flecked with numerous blood spots of about pin-head size. The sectioned surface is white, whorled and very tough. The uterus contains two small subperitoneal and one interstitial fibroid at the fundus and an endometrial polypus, but is otherwise normal. Tubes normal. Section of the right ovary (fig. 1) and left ovary shows typical serous adenofibroma on either side. At certain areas on the surface of the ovary and of the more substantial clefts are seen groups of acini of a wavier outline surrounded by a loose but cellular stroma more or less infiltrated with blood. These are interpreted as endometriosis (figs. 2, 3 and 4). In the case of one of these areas it can be seen that the entering connective tissue fibres alter, becoming finer, more subdivided and less disposed to occur in bundles. There is also seen a ripening follicle and what is interpreted as an atretic follicle with a luteinized theca interna.

There is no evidence of old hæmorrhage and the prussian-blue reaction is negative except for traces of iron in the wall of the atretic follicle. The endometrium is in the follicular phase and contains some mitoses.

*Discussion*.—The adenofibroma was presumably present before the menopause when the enlarged left ovary was first felt. It is unlikely that the endometriosis was present then, as no adhesions or other typical indications of its presence were



FIG. 1.—Serous adenofibroma.  $\times 40$ .



FIG. 2.—Local development of glands and stroma suggesting endometriosis.  $\times 40$ .



FIG. 3.—Detail of fig. 2.  $\times 160$ .



FIG. 4.—A large cleft in left ovary showing a nodule of metaplasia to endometriosis.  $\times 13$ .

found at operation. The negative prussian-blue reaction further makes it unlikely that it had developed at the time of the single post-menopausal bleeding in May 1948. If it arose by implantation it must therefore have been at this time. Its intimate relation at numerous points with the adenofibroma and the direct continuity of the surface and glandular epithelia of the two conditions make such a supposition extremely unlikely. The serosal origin of both conditions, which the sections directly suggest, seems the only possible interpretation.

#### Pre-Invasive Cancer of the Cervix (Bowen's Disease). Report on Two Cases.—ROSA HERTZ, M.B.

These two cases were described because they were fairly typical of a lesion which, although identified relatively frequently in epithelia elsewhere in the body, has only rarely been seen in the cervix. They occurred within one month of each other at the Post-graduate Medical School of London. In each, the condition was diagnosed on a biopsy and confirmed on serial sectioning of the removed cervix.

The first patient was a parous woman of 63, ten years post-menopausal, who was admitted with the complaint of vaginal bleeding of three months' duration. The only significant finding was a grossly eroded cervix. Biopsy of the cervix showed an intra-epithelial pre-invasive carcinoma to be present. Hysterectomy and bilateral salpingo-oophorectomy were performed, this lesion being radio-resistant.



The second patient was a parous woman of 51, three years post-menopausal, who had had very slight vaginal bleeding on occasions for eighteen months. For the past six weeks she had been experiencing post-coital bleeding. Examination revealed a polyp, the size of a pea, protruding through the os uteri. This was removed and histology showed "extreme pre-cancerous hyperplasia which can be classified as 'Bowen's disease'." Operation was carried out as in the previous patient and the pre-invasive carcinoma demonstrated in serial cervical blocks.

**Extramembranous Pregnancy.**—MARY K. LAWLOR, F.R.C.S.Ed., M.R.C.O.G.

There are many cases of extramembranous pregnancy on record. The remarkable feature of this case is that the pregnancy reached 34 weeks' maturity without causing irremediable contractures of the limbs, and the child, who is now 7 months, gives promise to develop as any other normal child except for some muscular stiffness.

The main interest in the condition lies in its correct ante-natal diagnosis. The mother was admitted to hospital with signs and symptoms of threatened miscarriage at 10, 14, 21, and 24 weeks respectively. On each occasion the character of the blood-stained discharge was noted as being unusually watery but this was ascribed to a bleeding cervical erosion in addition to a hydorrhœa gravidarum and some separation of the decidua or placenta. At 30 weeks' maturity the discharge was a little more heavily intermingled with blood and the patient was admitted with a diagnosis of placenta prævia, and threatened premature labour. The uterus was observed to be a little smaller than was consistent with the date of maturity and was unusually tense and irritable, the presentation was persistently a breech and the foetal movements were restricted. An X-ray picture showed the spine to be flexed, but not crumpled. This latter characteristic coupled with audible foetal heart sounds ruled out intra-uterine death. About this time a small piece of necrotic amniotic membrane was passed. This suggested the diagnosis of a retained undeveloped twin.

At 34 weeks' maturity labour commenced and progressed to a spontaneous delivery of a breech presentation of a live female premature infant showing unusual rigidity of the limbs, in an attitude of flexion. The head was moulded obliquely and the mouth, which was large in proportion to face and head, tended to remain open and contained mildly adherent blood clot. There had been no evidence of a bag of waters nor had there been a sudden gush of liquor during the labour.

The infant Susan weighed 4 lb. 7 oz. and after a little difficulty in establishing respiration progressed normally. The only remaining deformity was a talipes equinovarus of the right foot and a metatarsus varus of the left. Lactation was not satisfactory, probably due to a mild degree of uterine sepsis for which the mother was given penicillin, and to which she reacted very violently with urticaria and pyrexia. Susan from here onwards was fed with a spoon as she did not take kindly to a bottle. I sent her to Mr. Denis Browne at Great Ormond Street for an opinion on the deformities and she has been treated by him ever since. He gives a very good prognosis, but states that the muscular tone is poor and it is likely that Susan may always have a certain degree of stiffness but with treatment this will improve and probably be no handicap. She now weighs 14 lb., is a normal baby and bids fair to grow up to be a normal child.

As far as I can discover in the literature she is the only child developed extramembranously who has survived for so long a period. This must be partly due to the ante-natal care in helping the mother to carry on the pregnancy to 34 weeks' maturity, and to the delivery at 34 weeks before the contractions became too fixed. Also to the care given to Susan by her mother, who has been a most devoted nurse.

The following specimens were also shown:

**Endometrioma of the Round Ligament.**—MR. J. B. BLAILEY.

**Volvulus of the Pelvic Colon Simulating a Concealed Accidental Hæmorrhage.**—

MR. BRIANT EVANS.

**Physometra associated with Constriction Ring.**—DR. GEORGE C. BRETNALL.

## Section of Neurology

President—WILLIAM JOHNSON, M.C., M.D., F.R.C.P.

[November 4, 1948]

MEETING HELD AT THE NATIONAL HOSPITAL, QUEEN SQUARE, LONDON

**Persistent Rhythmic Contractions of the Ipsilateral Pharynx, Larynx, Vocal Cord, Face and Arm Following Trauma.**—G. MILTON SHY, M.R.C.P., and E. ARNOLD CARMICHAEL, F.R.C.P.

*History.*—Captain X, in order to avoid repatriation proceedings undertaken to return him to the jurisdiction of a foreign country, attempted suicide by projecting an ordinary lead pencil into the skull by way of the right orbit. Before losing consciousness he had projected this pencil an estimated 15 cm. He was unconscious for forty-eight hours except for "a brief island" of a few seconds *en route* to hospital where no surgical interference was taken other than the removal of the pencil. On regaining consciousness he found he could no longer exert control over the right arm and leg; this was profound for some two months, then rapidly improved. The motor disability was chiefly that of maintaining balance in walking and a clumsiness and loss of former dexterity in the right hand. He tends to fall to the right. He has now in addition noticed some coarse tremor of the right hand on voluntary movement. Since the injury he has had a constant pain on the entire left side of the body including the face and head. This has not improved and is what he describes as a feeling of heat or scorching of the surface. He cannot discriminate finer differences of temperature on the left side, but has not burned himself. He is aware of a constant clicking noise in the right ear. Since wounding he has been totally blind in the right eye.

On examination, one finds a man of normal intelligence with no speech defect, but with complete loss of vision in the right eye. Ophthalmoscopically the right optic nerve is dead white with a deposition of pigment at its lower inferior margin; the retina is normal but the arteries are narrow. Vision of the left eye is 6/6 and the fundus is normal. There is slight ptosis of the right upper lid. The right pupil is larger than the left, and fixed to both light and accommodation-convergence reflexes: the left and right consensual reactions are absent. There is no defect of ocular movement and no nystagmus. Hypalgesia is present over all three divisions of the left trigeminal area, and temperature discrimination is similarly affected; light touch is accurately perceived but not felt "as strongly" as on the right side. There is a rhythmical movement at 3–5 per second of the orbicularis oris involving the right cheek muscles and both upper eyelids. The palate at rest is held a little over to the right and the right fold appears shorter and more highly arched than the left. This side of the palate is the seat of constant twitching at about 180 per minute. The movement consists of a quick jerk to the right and then what appears to be a slow return to the mid-line not unlike saw-tooth nystagmus. On phonation the palate is drawn to the right and the right posterior pharyngeal

wall shares in this movement, becoming more wrinkled than the left. There is a coarse involuntary rhythmical tremor of the right hand accentuated by movement: there is a slight hypotonia in the right arm. There is excessive rebound of the right arm; repetitive movements are clumsy on the right; the left shows normal co-ordination. No marked weakness in either arms or legs is present. The plantar responses are flexor. Light touch is felt accurately but tickle is depressed on the left side: there is also a slight but definite hypalgesia and hypothermia on that side. Vibration and joint sense are normal. Special laryngeal examination shows adduction contractions of the right vocal cord at 160 per minute not clearly synchronized with those of the pharynx. In the diaphragm no myoclonus of any nature is to be determined. His gait is wide-based and uncertain.

**Familial Myoclonus and Congenital Morbus Cordis.**—FRANK A. ELLIOTT, F.R.C.P.

J. H., aged 44, sought advice for pain in left arm, paræsthesiæ in thumb, stiffness of neck and reduction of left biceps-jerk—a typical case of herniation of fifth cervical disc. Found to have congenital heart disease—Eisenmenger complex, with right ventricular preponderance on E.C.G.

Since early life has suffered from involuntary jerking movements of the legs, sufficient to displace the limb violently and usually taking the form of a contraction of quadriceps. The resultant "kick" is sustained for some seconds by myoclonus. These movements are limited to the legs, are aggravated by warmth and by lying down, are absent during voluntary movement, and are relieved by cold. They start with tingling in the side of the foot. Consciousness not disturbed. No fits. Quite well otherwise.

Father suffered from precisely similar symptoms but he, too, was free from epilepsy. The only abnormality in the nervous system was generalized exaggeration of the tendon-jerks.

There is no myotonia.

The E.E.G. is normal at rest and after overbreathing. The predominant frequency was 10 per second and distribution was normal.

**Diagnosis.**—The sustained nature of the involuntary movements distinguish this case from the simple "jumping" of the legs seen in many normal persons and also in epileptics. The case appears to be one of familial myoclonus without epilepsy.

**Abnormal Ocular Movement.**—FRANK A. ELLIOTT, F.R.C.P.

Violet H., aged 17, came under observation in March 1948 as a case of mild acute glomerular nephritis following streptococcal tonsillitis. Was found to have remarkable voluntary control of ocular movements, which she had discovered accidentally six months prior to the present illness. She is able to rotate or roll the eyes synchronously, in an anticlockwise direction, at the rate of from 2–3 per second. It is a continuous rotation, not a nystagmus. She initiates the movement by converging the eyes, and can stop it at will. The upper lids move up and down in time with the rotation, but so far as can be determined by the unaided eye, the pupils remain constant. While carrying out this movement she is aware that outside objects are "dancing". Unlike voluntary nystagmus, the movement is not stopped by placing strong lenses in front of the eyes.

The rest of the C.N.S. is normal.

**? Manganese Intoxication.**—MACDONALD CRITCHLEY, M.D., F.R.C.P.

Mr. A. D., aged 54. Brassfounder,

Seventeen months ago collapsed at work. He was admitted to hospital, and during the course of twelve hours had 7 typical epileptic attacks. It was discovered at that time that he had splenomegaly.

Twelve months' history of progressive loss of power in left hand and arm and increasing stiffness of the arm and fingers. Three months' history of weakness and dragging of the left leg.

Seven months ago he had suffered from frontal headaches for about three months.

**Examination.**—Intelligence shows moderate deterioration from an originally low average; the greatest defect being in memory. Expressionless face and monotonous voice.

Skew deviation of the eyes on deviation to the right—the right eye being elevated and the left depressed. Marked left lower facial weakness. Gait is slow. The left arm is held flexed and adducted; the left leg is held stiffly, the toes dragging on the ground and the whole limb is circumducted.

Marked rigidity of the left arm and leg of a plastic type. Gross weakness of finger flexors and rather less weakness of all other movements of the left arm and leg. Left arm-jerks slightly brisker than the right, left knee and ankle jerks similarly increased and the left plantar response is equivocal.

*Sensation*.—Moderate reduction in cutaneous sensibility and vibration sense down the left half of the body with sparing of the face. Loss of sense of passive movement in the left fingers and toes and some reduction in sense of passive movement at the larger joints. There is tactile and pain extinction on the left side to gross stimuli applied simultaneously to both halves of the body. Gross astereognosis in the left hand and loss of two-point discrimination and localization in the left hand and foot. Greatly enlarged spleen, liver just palpable but soft and smooth. Blood-pressure 130/80.

X-ray of skull normal.

Electro-encephalogram: Shows random low voltage waves at 2 c/s. over the right hemisphere with no accurate localization.

Air encephalogram: Shows moderate dilatation of the right lateral ventricle.

C.S.F.: Normal pressure, cytology, chemistry and serology. Blood W.R. negative.

*Blood-count*.—R.B.C. 5,550,000; Hb 102%. W.B.C. 8,000 (polys. 74%, lymphos. 19%, monos. 1%, eosinos. 1%, basos. 5%).

Liver function tests all normal.

## ? Peduncular Hallucinosis.—MACDONALD CRITCHLEY, M.D., F.R.C.P.

Mrs. E. M. S., aged 47. Housewife.

Two years' history of a severe, bursting, vertical and occipital headache associated with vomiting; these headaches usually occurred with her menstrual period. Two attacks of confusion followed by amnesia for the event, each attack lasting three to four hours (one eighteen months ago and the second two months ago).

Two months' history of failing vision, left more than right. Associated with the visual failure but following it she has had visual hallucinations of a highly organized character. They always occurred in the lower left quadrant of her visual field, and have taken the form of various animals, highly coloured, correctly proportioned, but always miniature.

In addition they frequently take the form of distortion or of perseveration of an existing pattern across her field of vision. Railings on her left side appear to be projected across the street and curtain patterns across the walls.

*Examination*.—V.A.R. 1/36. V.A.L. less than 1/60. The right field shows a relative nasal defect to small objects on the left side. There is almost a horizontal upper defect with greater sparing of vision in the lower temporal quadrant. Fundi: Moderate bilateral papilloedema. The left pupil reacts poorly to direct light but reacts briskly consensually. All the tendon reflexes are exaggerated and the plantar responses are flexor.

E.E.G.: In all areas there is low voltage, random, irregular, slow activity. On the left side spreading somewhat to the right, and more frontal than occipital, there is an 8 c/sec. rhythm, fairly continuously present, and tending to occur in outbursts of increased amplitude associated with 4–5 c/sec. waves.

Overbreathing increases this 4–5 c/sec. activity, and makes it more markedly left sided.

X-ray of skull: Sella shows complete destruction of clinoid processes and dorsum and some erosion of the anterior wall of the sella and of the right lesser wing sphenoid; the right optic foramen could not be clearly defined.

## Generalized Neurofibromatosis with Intracranial Mass and Pulsating Enophthalmos.—R. E. KELLY, M.D., M.R.C.P. (for S. P. MEADOWS, M.D., F.R.C.P.).

W. H., aged 24. Soldier.

Mother had neurofibromatosis and died of cerebral astrocytoma at age of 54,

*Patient's history.*—History of squint since infancy, progressive loss of vision in left eye for five years, and supra-orbital headaches for three months.

*Examination.*—Generalized neurofibromatosis and café-au-lait patches. Visual acuity—left eye— $1/60$  with large nasal field defect. Left optic disc myopic. Congenital abnormality of left iris. Left sixth and partial third nerve paresis, and left pulsating enophthalmos.

*Investigations.*—X-ray of skull shows gross elevation of left sphenoidal ridge, gross enlargement of the pituitary fossa; enlargement of the left orbit and a defect in the greater wing of the sphenoid on the left side.

Electro-encephalogram shows no abnormality.

Left arteriogram suggests large space-occupying lesion on the left side of the sella, displacing the carotid siphon forwards, downwards and medially.

The opinion of members was asked as to the nature of the space-occupying lesion and the treatment recommended.

### Facial Palsy, Bilateral.—DENIS WILLIAMS, M.D.

Mrs. E. H., aged 30.

*Past history.*—Right-sided tuberculous adenitis when aged 6. Scarlet fever, otorrhœa and jaundice at the age of 10. September 1947: Acute appendicitis which was followed by recurrent abscesses on the scar. These did not clear up until December 1947. Since then has had about a dozen attacks which she likens to influenza in which she shivers and feels unwell for about four days.

*Present complaint.*—August 8, 1948: Shivering attacks with transient pain in the left ear. Three days later woke and found she was unable to move the left side of her face and could not feel objects touching her on that side. August 13: Diplopia on looking to the left. Treated with penicillin with rapid improvement. The weakness and diplopia cleared up in about a week and the facial palsy in about two months.

10.9.48: Examination at the National Hospital, Queen Square: No abnormality except a recovering left lower motor neurone facial palsy. The fifth and sixth cranial nerves had recovered. X-ray of skull normal.

22.10.48: On waking was unable to move the right side of the face.

24.10.48: Whole of the right side of the face acutely tender necessitating injections of morphia.

*Present condition.*—Afebrile. Right lower motor neurone facial palsy. Taste preserved. Oculomotor nerve normal. Fifth nerve acutely tender on pressure in the area of distribution of all three divisions on the right side. Corneal responses brisk and equal. Eighth nerve—hearing unaffected, drums clear.

*Investigations.*—Blood-count: R.B.C. 4,850,000; Hb 88%; W.B.C. 6,400 (polys. 50%, lymphos. 48%, monos. 2%). B.S.R. 3 mm/hr. Urine: No abnormality. E.E.G. normal. C.S.F.: pressure 110 mm.; normal constituents; W.B.C. 5; protein 30 mg.%; Lange 0000000000.

X-ray of skull normal. No change in internal auditory meati nor in sphenoidal ridges.

The patient was treated with intramuscular injections of penicillin 100,000 units four-hourly. The pain and tenderness subsided but the facial palsy remained unchanged. She was re-examined on December 7, 1948, and her condition was stationary.

It is presumed that in this case infection residual from the appendix abscess and causing the rigors had involved the right and then the left petrous bone. It is very difficult to see how infection could track from one petrous to the other without involvement of venous channels and possibly of the cavernous sinus which seemed to be unaffected. The possibility of a basal meningitis was considered but there have been no signs of intracranial infection. The diagnosis of polyneuritis cranialis has no value, but the actual cause of the bilateral cranial nerve palsies in this case is obscure.

### Blindness, Ophthalmoplegia and Sensory Polyneuritis.—DENIS WILLIAMS, M.D.

L. H., aged 58. Printer's assistant.

Came to the National Hospital in mid-September because he had gone blind in his left eye.

*History.*—14 weeks: Bifrontal shooting headaches. 13 weeks: Severe ache deep in the

thigh, hamstrings and calf, especially the right. Not made worse by coughing or back movement. 12 weeks: Some numbness in the left thumb and forefinger. 11 weeks: Vision on the left rapidly began to deteriorate without pain. 7 weeks: Constipation. He was then seen at the National Hospital when he had light perception only on the left. The pupil was sluggish and the corneal reflex diminished. Elsewhere the nervous system was normal, reflexes being present. 6 weeks: Pain in the legs more severe. He had become blind in the left eye and sight in the right was rapidly deteriorating. Urinary frequency and dribbling incontinence. 5 weeks: Quite blind.

*Past illness.*—Thirty years previously lupus vulgaris of the neck, healed with treatment.

*Examination on admission.*—Cachectic evidences of old lupus in the neck and ears. The bladder was disturbed, there was retention with overflow but no other disorder could be found in any system apart from the C.N.S. There was no evidence of a malignant mass or enlarged glands on full examination. He was alert and co-operative. The following abnormalities were present:

*Cranial nerves:* He was absolutely blind, the pupils being fixed, the optic discs normal. Complete third and fourth nerve palsy in the right. Corneal reflexes very sluggish, sensation being intact in the face. Hearing diminished on both sides equally.

*Motor system:* Muscles tender. Generalized wasting, power fairly good, tone normal, reflexes absent in the arms, unequal and sluggish in the knees and absent at the ankles. No fasciculation.

*Sensation:* Peripheral type of sensory loss to all forms.

*Other systems:* Apart from some coarse crepitations at both pulmonary bases, no significant abnormality was found.

*Progress.*—Since admission the cranial nerves have remained unchanged except for organized visual hallucinations to the right. In the past week his knee-jerks have disappeared and the peripheral sensory loss has extended and intensified.

*Investigations.*—X-rays of skull, bones, and alimentary tract normal. X-rays of chest showed a small shadow in the mid-zone of the left lung which on tomography was suggestive of a small primary lung carcinoma.

E.E.G.: The dominant frequency was only 7 a second. No focal abnormality was seen.

Sedimentation rate (6.10.48): 16 mm. in the first hour.

Blood W.R. negative.

C.S.F., 4.10.48: Protein 250 mg. Cells 60 per c.mm. (60% lymphos.). 12.10.48: Protein 300 mg. Cells 60 per c.mm. (70% lymphos.).

Lange: No change. W.R. negative.

Full blood-count normal.

The differential diagnosis in this case was thought to rest between sensory neuropathy with secondary carcinomatosis, as described by Denny-Brown, or secondary carcinomatosis of the meninges.

*POSTSCRIPT.*—After the case had been presented the patient's condition slowly deteriorated and he died. The autopsy report (Dr. J. Godwin Greenfield) read:

On the dura mater there was thickening on the left side anteriorly of the foramen magnum on the optic tubercle and on several small areas which were attached to the underlying brain tissue, there were small thickenings apparently of carcinoma. One was present over the conus terminalis on the dorsal surface of the cord, where the dura mater was attached to the nerve roots by a nodule of growth. The brain was tense under the dura mater and herniated into the lateral sinus along the point of entrance of the posterior anastomotic veins. Nodules of growth were present on the right third nerve just before it entered the cavernous sinus and in its course in the cavernous sinus it was diffusely swollen. Both optic nerves, especially the right, were also diffusely swollen behind the optic foramina.

No evidence of growth on the eighth nerve was visible. A soft white mass of growth filled the left cerebellar tonsil, and a smaller one lay in the mesial surface of the right tonsil. A small area of growth was present on the surface of the cerebellum as well as one or two attached to the dura posteriorly.

In the spinal cord a nodule of white growth lay on the left first thoracic root.

Neck and chest: A swollen gland the size of a large haricot bean lay on the left side of the trachea just below the thyroid which was normal.

Lungs not adherent. Right lung normal, weight 430 grammes. Left lung, upper lobe in a condition of pinkish-grey hepatization with granules of whitish material which represented the alveolar exudate on the cut surface about one inch from its lower margin (interlobar fissure) there was a cavity surrounded by a friable whitish wall. No solid cancerous growth was seen here.

There was, however, much infiltration, chiefly with small white nodules of growth, but in places by more solid white tissue of the glands at the left hilum and below the bifurcation of the bronchus. Weight of left upper lobe 800 grammes, lower lobe 285 grammes.

Heart and aorta healthy.

Stomach showed a puckered area near the pylorus in the lesser curvature, but no ulcerations present.

Intestines normal.

Liver: Weight 1,790 grammes. Normal.

Spleen: Weight 85 grammes. Pale and congested and diffuent.

Suprarenals normal. No infiltration.

Kidneys large. Weight 365 grammes. Pelvis and ureters inflamed.

Bladder-wall inflamed with a diverticulum with rather a wide orifice near the fundus.

Prostate not enlarged and quite soft. No secondary growths were seen in the abdominal cavity.

Further examination of the spinal cord after fixation showed small deposits of growth on the dorsal root ganglia or near the exit of the spinal nerve roots of the left C.4 and C.6 and Th.1, and also of the right C.5 in addition to the deposits on the roots of the cauda equina already noted. Many of the dorsal root ganglia were firmer than normal and rather swollen in an irregular manner by nodules of growth especially in relation to the cauda equina where there were also plaques or nodules on the inner surface of the dura mater. The right optic nerve, on section, was found to have a central nodule of growth. The left optic nerve also contained a smaller eccentrically placed nodule.

The retina, on section of the eyeball, appeared normal.

## Section of Laryngology

President—E. COWPER TAMPLIN, M.C., F.R.C.S.Ed.

[November 5, 1948]

### The Last Ten Years—Some Experiences and Reflections. [*Abridged*]

#### PRESIDENT'S ADDRESS

By E. COWPER TAMPLIN

#### POLIOMYELITIS AND TONSILLECTOMY

A MEMORANDUM by Medical Officers to the Ministry of Health in the *Brit. med. J.*, 1947 (ii), 141, advised postponement of tonsillectomy whenever possible during the prevalence of poliomyelitis. At the Cambridge B.M.A. meeting, according to the printed report, the same view was put forward by two or three speakers, but was questioned by laryngologists who were present.

It is time therefore to enquire on what grounds and on what evidence this "stoppage" is advised. I have endeavoured to do this and would like to record some of my investigations.

First a word on statistics. They are useful and necessary, but we should be as careful in drawing conclusions from them as we should be from an array of selected opinions. Both can be made to prove anything.

Here three examples were given (*see* refs. 1 and 2), and the speaker continued:

The last example (ref. 2, p. 1227) shows that cases of otitis media had already fallen from 80 to 30 (more than 50%) TWO YEARS BEFORE the reductions in tonsillectomies. Yet on that evidence we are told, only this year [3] that "Similar reductions in the cases of otitis media followed even more drastic reductions of tonsillectomies by Garrow of Hornsey". Note the word "followed".

These examples show to what conclusions statistical evidence alone may lead. It is surely obvious there are other factors which must be taken into consideration and we should only use such evidence in conjunction with practical knowledge and experience.

The Monthly Bulletin of the Ministry of Health for July 1948 contains an impressive article on the subject. I am grateful to the editor (Dr. J. Alison Glover) for having kindly sent me a copy.

It should be noted that in this article two of the references are not connected with poliomyelitis and of the remaining 15, no less than 14 are American. I had already read most of them and I would draw your attention to six others, which, I suggest, give a different picture (*see* refs. 1, 4, 5, 6).



Lungs not adherent. Right lung normal, weight 430 grammes. Left lung, upper lobe in a condition of pinkish-grey hepatization with granules of whitish material which represented the alveolar exudate on the cut surface about one inch from its lower margin (interlobar fissure) there was a cavity surrounded by a friable whitish wall. No solid cancerous growth was seen here.

There was, however, much infiltration, chiefly with small white nodules of growth, but in places by more solid white tissue of the glands at the left hilum and below the bifurcation of the bronchus. Weight of left upper lobe 800 grammes, lower lobe 285 grammes.

Heart and aorta healthy.

Stomach showed a puckered area near the pylorus in the lesser curvature, but no ulcerations present.

Intestines normal.

Liver: Weight 1,790 grammes. Normal.

Spleen: Weight 85 grammes. Pale and congested and diffuent.

Suprarenals normal. No infiltration.

Kidneys large. Weight 365 grammes. Pelvis and ureters inflamed.

Bladder-wall inflamed with a diverticulum with rather a wide orifice near the fundus.

Prostate not enlarged and quite soft. No secondary growths were seen in the abdominal cavity.

Further examination of the spinal cord after fixation showed small deposits of growth on the dorsal root ganglia or near the exit of the spinal nerve roots of the left C.4 and C.6 and Th.1, and also of the right C.5 in addition to the deposits on the roots of the cauda equina already noted. Many of the dorsal root ganglia were firmer than normal and rather swollen in an irregular manner by nodules of growth especially in relation to the cauda equina where there were also plaques or nodules on the inner surface of the dura mater. The right optic nerve, on section, was found to have a central nodule of growth. The left optic nerve also contained a smaller eccentrically placed nodule.

The retina, on section of the eyeball, appeared normal.

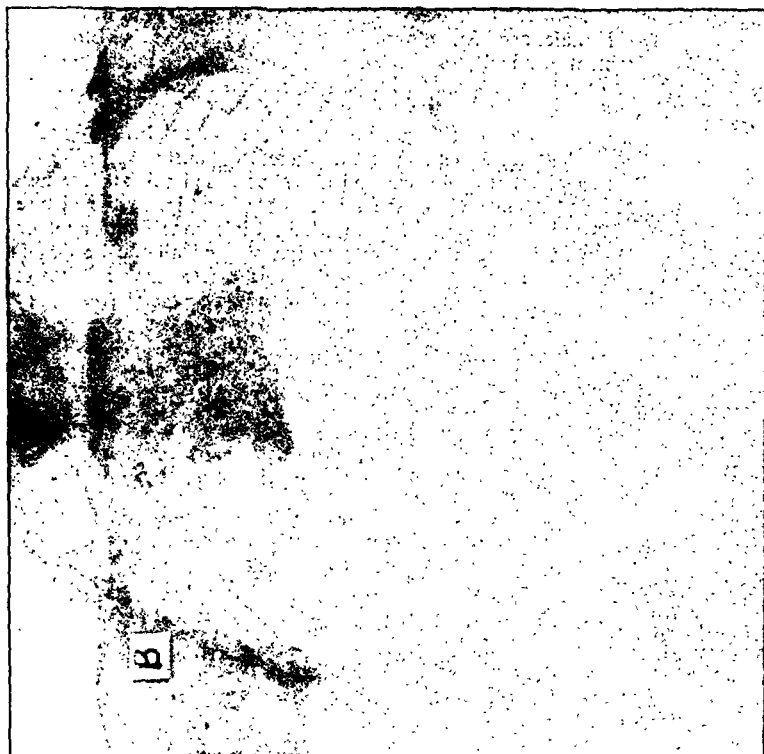


FIG. 2.—Widespread secondary carcinomatosis with very much larger shadows than those seen in fig. 1. No clinical signs or symptoms.

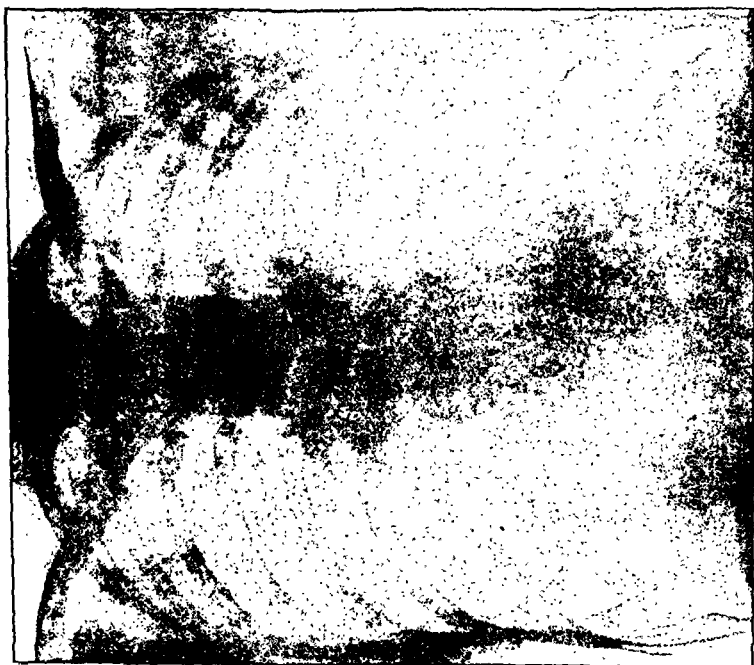


FIG. 1.—An interesting picture of miliary tuberculosis. No definite clinical signs or symptoms. A "snow-storm" with a multitude of very fine, small shadows in both lung-fields. Compare with fig. 2.

There can be little doubt that the majority of tonsillectomies are not elective: most of them are necessary surgical procedures, performed in the interests of preventive medicine: and I must agree with the conclusions of the more recent authors that the incidence of poliomyelitis in tonsillectomized individuals is no greater than in those individuals whose tonsils have not been removed.

In this country poliomyelitis cases following recent tonsillectomy were fewer than might have been expected from some American experiences and it has been suggested this was because we were alive to the danger, but surely so were the Americans for they had begun to consider it nearly forty years ago!

The questionnaire sent out to hospitals by the Ministry of Health in October 1947 did not include a question on tonsillar state. This was unfortunate, for poliomyelitis has been with us a long time and in Portsmouth, at least, the visitation of 1938 was in some respects more serious than that of 1947, yet we never stopped our ordinary lists, but adopted the arrangement I shall mention shortly.

What justification is there for general postponement? In my opinion there is no doubt whatever that if we unnecessarily postpone operating, great harm, needless suffering and serious ill-health will result to hundreds of children who are in sore need of our assistance. Meanwhile something on the lines of our procedure in Portsmouth and district might be adopted, as I do not know of any authoritative BRITISH evidence.

### *Portsmouth Experience*

Our experience is small but not uninteresting. In 1947 well over 1,000 tonsillectomies were performed in the City alone. 82 cases of probable poliomyelitis were admitted to the Infectious Diseases Hospital, 31 of which proved to be definite. Four cases were fatal, all of which exhibited signs of bulbar involvement. None of these 82 cases had been tonsillectomized recently. I know this because the Medical Superintendent of the I.D.H. and his deputy on their own initiative had examined these cases as to recent tonsillectomy.

Close co-operation exists between them and ourselves, so that should occasion arise, joint consideration can be given at once to the question of postponement of operation.

### X-RAY FILMS

Films of 4 Cases were shown, 3 of which are illustrated

I.—Male, aged 61, complained of "something in his throat"; no cough and he appeared fit. On examination the right tonsil was enlarged, irregular, ulcerated and the surrounding tissues were not invaded; no cervical glands.

I had no doubt it was an epithelioma and dissected out the tonsil with a diathermy needle. The pathological report was: "The specimen consists of an enucleated tonsil, measuring  $3 \times 2 \times 1$  cm.

The surface is ulcerated and on bisection there are areas of firm, opaque, white tissue. Section shows the lymphoid tissue to contain numerous typical tubercle follicles with some caseation. In sections stained by Ziehl-Neelsen's method acid-fast bacilli can be seen in considerable numbers."

The physicians were asked to see him and found nothing clinically but an X-ray of his chest produced the film shown—the best X-ray photograph of military tuberculosis I have seen. The tonsil bed was healed in twelve days, he was put on streptomycin, has gained 12 lb. in weight, but is not doing well (see fig. 1).

II.—Male, aged 68, was referred to me because five or six times in the last month his throat "seemed to close up suddenly when eating". It was only momentary and he finished his meal normally.

On examination, pharynx, larynx, post-cricoid region and pyriform fossæ were all normal, but he LOOKED ill and I therefore had him X-rayed with the result shown in fig. 2.

He never had any cough, difficulty in swallowing or pain, but gradually became weaker and died seven weeks later.

X-ray report: "Obstruction in œsophagus at level of aortic arch, outline in keeping with malignancy. There is widespread secondary carcinomatosis in both lung fields" (see fig. 2).

Both these cases had no chest symptoms or clinical findings and the very fine shadows of the military tuberculosis are in marked contrast to the very much larger ones of carcinomatosis.

embryonic remains of the notochord and is still a comparatively rare condition.

The first case of spheno-occipital chordoma to be recorded in the British Isles was that of Burrow and Stewart [13].

Since then Gavin Livingstone [14], Gould [15], Carnegie Dickson, Worster-Drought and McMenemey [16] have reported cases and in 1943 I showed at this Section a man of 38, referred with a six months' history of "a completely blocked nose, loss of taste and smell and recent difficulty in swallowing; hearing in both ears normal".

There was a very large, firm, reddish mass in the nasopharynx pushing the soft palate forwards and downwards to the limit. A short course of deep X-rays caused no improvement.

Two months later I removed the growth through a transverse incision at its lower border. I had not decided whether to take a portion for biopsy or try for total removal, but as the latter seemed possible I went ahead. The mucosa stripped easily anteriorly and laterally, but posteriorly the mass was bound down very firmly.

After attempts to remove it whole I adopted a morcellement procedure with Luc's and Behnke's forceps and this was successful though postero-superiorly there was one area about 1 in.  $\times$   $\frac{1}{2}$  in. where bare, rough bone could be felt. The overlying tissues were replaced and a postnasal plug was inserted for twenty-four hours in case of hæmorrhage. Recovery was uneventful and he left hospital two weeks later.

Dr. J. D. Radcliffe, our pathologist reported: "This tumour consists of rather large cells which are grouped in small masses by strands of loose connective tissue. The tumour cells frequently show large vacuoles containing mucin and they are often surrounded by more or less mucin, acting like an intercellular substance. In a few places the cells appear as a syncytial mass. The tumour is a CHORDOMA".

The patient gained 2 stones in weight and did light work but gradually it became obvious that intracranial invasion had begun and eighteen months after I had first seen him he was admitted to hospital in a dying condition. At post-mortem a large mass was removed from the base of the skull, arising from the spheno-occipital synchondrosis.

#### *Papillomata of Larynx*

A child aged  $2\frac{1}{2}$  years was brought to hospital with very great difficulty in breathing. The mother said it had begun four months previously and had gradually become worse.

On examination there was marked indrawing at the suprasternal notch and around the clavicles, in the intercostal spaces and at the epigastrium.

On direct laryngoscopy all that could be seen was an irregular raspberry-like mass practically filling the whole glottis. An immediate tracheotomy was done. For two or three days he developed a mild pneumonia which cleared with penicillin. He had several "attacks" in which respiration stopped and the pulse was imperceptible but coramine restored him. However he died in one of these attacks seven days after admission, apparently because the four months' strain was too much for the heart.

In *J. Laryng.*, 1948, 62, 621, in an article on this condition, Zalin' suggests treatment by local application of œstrogen which shows some promise.

In my experience papilloma of the larynx occurred occasionally before the war, but this is the only case I have seen in the last ten years, with the exception of a tracheotomic fistula which remained from previous treatment of one and which I closed so that the lad could join the R.A.F.

#### *Hæmangio-endothelioma of Trachea*

This specimen was from an infant of 4 months who was moribund when admitted to hospital and died before anything could be done. It is the only specimen that survived the "blitz". I show it only because of its rarity.



FIG. 3.—Many attempts were made to obtain radiological evidence, but this was the only successful picture, showing a very temporary stricture with a pear-shaped dilatation above, which passed off completely in a few moments.

### III.—Stricture of œsophagus.

Female, aged 31. Married. Referred with a year's history of intermittent difficulty in swallowing and occasionally regurgitation. Screened and X-rayed with barium several times but nothing definite found.

Œsophagoscopy: normal, except for quite small slightly red areas at 24, 28 and 32 cm. She was therefore transferred to the medical wards where neurological and all other examinations were negative. X-rayed again and on the second occasion (fig. 3) the picture was obtained. In a few minutes she said "It's gone" and another film taken in the Trendelenburg position showed all the barium in the stomach with no sign of returning to the œsophagus. With careful dieting and reassurance she was sent home and is still improving. It is interesting that her mother and aunt have somewhat similar symptoms: the mother has an œsophageal pouch, but the aunt refuses to be X-rayed.

### ABSCESS-TONSILLECTOMY

Here I am going beyond the ten years for the sake of continuity and have included cases done in the Army in the last war.

I first became interested in this procedure about 1930 following some correspondence in one of our journals and an article by Canuyt [7] who incised the abscess and followed this by a tonsillectomy in some cases, but not as a routine procedure.

Thacker Neville [8], Linck [9], Heindl [10], and Swart [11] have all published papers on the subject and the last three consider "it should now be the operation of choice", "in no case was the procedure harmful or had given rise to any complication" and "the dangers of operating upon acutely inflamed tissue had been greatly exaggerated, at least in this field".

My own experience has been as follows:

I have now dealt with over 200 singles and 6 doubles without any complication arising. The patients themselves are very delighted with the relief from pain and discomfort and are extremely pleased they will not have to return for another operation at a later date. In these days when, in most areas, beds are precious, the reduced time in hospital is also a consideration. The majority of the patients are taking food with very little discomfort the next day and go home in a week or less.

Even the worst case, a double, where owing to the great œdema and swelling causing dyspnœa the house surgeon was advised by the doctor to have a tracheotomy set ready, the patient was discharged in ten days.

The extraordinary thing is that hæmorrhage is less than that occurring in ordinary tonsillectomy. I have never had to use a ligature or suture, but I do inject coagulen locally when required. In only two cases has it been necessary to deal with reactionary bleeding and then it has been on the NON-quinsy side! With an electric sucker, a good anæsthetist and an intratracheal tube there is no difficulty and the patients are practically "round" when they leave the table.

Notes on a few cases of interest, with specimens:

### *Chordoma*

In the basilar part of the developing occipital bone the notochord approaches the lower or pharyngeal surface of the bone and part of it may lie between the basilar plate and the wall of the pharynx [12]. A chordoma is a tumour arising from the

## Section of Pædiatrics

President—Professor J. M. SMELLIE, O.B.E., M.D., F.R.C.P.

[October 22, 1948]

**Partial Hemihypertrophy Affecting Right Leg.**—J. R. D. WEBB, O.B.E., M.R.C.P., D.P.H., D.C.H.

Girl, aged 22 months.

First seen in April 1947 when the right leg was much larger than the left. The hypertrophy affects the right leg only.

During the sixteen months the child has been under observation, growth and general development have been normal, her clinical condition has remained good and there has been considerable improvement in the abnormality.

**Albers-Schönberg Disease.**—S. B. DIMSON, M.D., M.R.C.P.

J. S., female, admitted to Queen Mary's Hospital, Stratford, in May 1948 at the age of 6½ months with hydrocephalus, snuffles, enlarged liver and spleen, and apparent blindness. Snuffles had been present since she was 4 weeks old and conjunctivitis (improving) since birth.

*Past history.*—Birth-weight 7 lb., normal pregnancy and delivery. Bronchitis.

*Family history.*—Parents not consanguineous. Mother's first pregnancy resulted in a miscarriage, second was normal, followed by birth of patient. Mother's blood: W.R. negative, Rh factor positive. Father had 2 greenstick fractures of right forearm before he was 14 and ? left Colles's fracture at 24. X-ray of both his forearms and skull showed no osteopetrosis but there was bowing of the proximal third of the right radius and ulna. Mother's left humerus, right tibia and fibula, and skull normal.

*Physical examination.*—Hydrocephalus, enlarged veins of scalp, head circumference  $17\frac{3}{8}$  in., anterior fontanelle bulging, parietal bossing, horizontal ridge in temporoparietal regions, marked projection of occipital region with a deep hollow underneath. No cranial nerve palsy. Aimless eye-rolling movements, apparently blind. "Rotatory nystagmus, pupils large and inactive to light, bilateral optic atrophy" (Mr. I. Spiro). Persistent snuffles, mild conjunctivitis. Moderate beading of costo-chondral junctions, Harrison's sulcus. Slight enlargement of cervical, axillary, and inguinal glands. Enlargement of epiphyses of long bones. Abdomen prominent, liver enlarged 2 fingers, spleen  $1\frac{1}{2}$  fingers. Small umbilical hernia.

*Investigations.*—I. Radiological (Dr. W. Johnston Craig).

Generalized increased density of entire skeleton typical of Albers-Schönberg disease.

(i) Skull: Base of skull and parietal region chiefly affected. Posterior clinoids are clubbed and sella turcica narrowed. There is no distinction between cortex and diploe (see fig. 1).

(ii) Ribs, clavicles, bodies of vertebræ and pelvis are uniformly dense (see fig. 2).

(iii) Limbs: Clubbing of ends of long bones, especially of proximal ends of humerus and tibia and distal end of femur. Density more marked at ends of bones. Fraying of proximal end of ulna, cupping and fluffiness of ends of shafts of long bones suggest active rickets. Periosteal elevations along shafts of left humerus, both femora and tibiae. No transverse bands seen. Centres of ossification normal (figs. 3 and 4).

(iv) Ring-like shadows of increased density at ends of metacarpals and phalanges of hands, less marked in metatarsals and phalanges of feet (see figs. 5 and 6).

### *Spasm of the Larynx in Infants and Children*

*Congenital laryngeal stridor.*—In the last three years I have had 6 cases of infants with a crowing or grunting or fluttering sound on inspiration noticed at birth or soon after. My obstetric colleagues also see them, but as the infants are never blue, usually grow and gain weight normally, I do not see them unless to satisfy an anxious mother.

On direct laryngoscopy there has been no web, but the upper orifice of the larynx is curved in on inspiration and is blown out on expiration. The infolding of the orifice is from side to side with a curling inwards and perhaps backwards of the epiglottis due to a flabbiness of the upper laryngeal aperture thus preventing full and free ingress of air.

The Jacksons have termed this laryngomalacia and consider it is due to a deficiency disease.

*Spasm of the larynx in children.*—This condition may also be due to dietetic errors or deficiencies, but one of the main causes is excessive secretion and such cases should be examined by a laryngologist.

Adenoids greatly increase the secretion in the pharynx which leads to an increase in the frequency and amount of secretion passing into the larynx. They also compel mouth breathing with its attendant inspiration of unfiltered, unwarmed air with consequent laryngeal irritation.

Therefore if adenoids are present, they should be removed before the child is dealt with by the physician.

*Laryngismus stridulus.*—This is rare after 3 years of age, but is more common to-day than before the war. In each case there is sphincteric closure with infolding of the laryngeal margins with no abnormal secretion or signs of inflammation. This again is probably due to a deficiency disease and the anatomic factor is laryngomalacia.

These 3 conditions appear to be increasing. The cause may arise in the mother or there may be some defect in the infants and children themselves. It may be due to lack of fats, deficiencies in the natural vitamin content of the food of to-day or to the chemical adulteration of the flour.

The ophthalmic surgeons tell me they are quite definitely meeting with a much greater incidence of minor troubles, such as corneal ulcers, blepharitis and conjunctivitis, which are taking much longer to clear up than before the war.

### REFERENCES

- 1 WINBORN, C. D., and STANSBURY, J. R. (1947) *Laryngoscope, St. Louis*, 57, 575.
- 2 GLOVER, J. A. (1938) *Proc. R. Soc. Med.*, 31, 1227 and 1229.
- 3 — (1948) *Arch. Dis. Childh.*, 23, 1.
- 4 CUNNING, D. S. (1946) *Ann. Otol. Rhin. Laryng.*, 55, 588 and 590.
- 5 AYCOCK, W. L. (1942) *Medicine, Baltimore*, 21, 65.
- 6 CUNNING, D. S. (1947) *Arch. Otolaryng.*, Chicago, 46, 575.
- 7 CANUYT, G. (1931) *Ann. Otolaryng.*, p. 61.
- 8 NEVILLE, W. S. T. (1936) *J. Laryng.*, 51, 650.
- 9 LINCK, A. (1936) *Arch. Ohr.-Nas.-, u. Kehlk-Heilk.*, 141, 255.
- 10 HEINDL, A., Jr. (1937) *Msch. Ohrenheilk.*, 71, 412.
- 11 SWART, G. J. (1947) Thesis, Leyden. 1-107.
- 12 WILLIS, R. A. (1948) Pathology of Tumours. London.
- 13 BURROW, J. LE F., and STEWART, M. J. (1923) *J. Neurol. Psychopath.*, 4, 205.
- 14 LIVINGSTONE, G. (1935) *Proc. R. Soc. Med.*, 28, 1427.
- 15 GOULD, S. E. (1936) *Arch. Otolaryng.*, Chicago, 23, 588.
- 16 DICKSON, W. E. C., WORSTER-DROUGHT, C., and McMENEMEY, W. H. (1937) *J. Path. Bact.*, 44, 41.



FIG. 5.—Increased density is more concentrated at the ends of metacarpals and phalanges.



FIG. 6.—The density is more uniform throughout the metatarsals.

## II. Laboratory (Dr. M. S. Ross).

Nasal swab: *Staph. albus* insensitive to penicillin. Blood W.R. negative, cerebrospinal fluid, splenic puncture, blood fragility, urine (repeatedly) normal. Clotting time  $1\frac{1}{2}$  min. (Lee and White's method), bleeding time 5 min., platelets 255,000. Peripheral blood shows a leuco-erythroblastic anaemia (see Table I). For blood chemistry see Table II; for urine chemistry see Table III.

TABLE I.—HÆMATOLOGICAL OBSERVATIONS

| Date                                                                                                                   | 15.6.48 | 10.7.48 | 26.7.48 | 18.9.48 | 20.10.48 |
|------------------------------------------------------------------------------------------------------------------------|---------|---------|---------|---------|----------|
| Hæmoglobin % (100% = 15.6 grammes)                                                                                     | 52      | 56      | —       | 60      | 62       |
| Red cells (millions/c.mm.) All showed aniso- and poikilocytosis, and chromatophilia +++ and also basophil stippling ++ | 2.82    | 3.34    | —       | 3.8     | 2.82     |
| Normoblasts (per 100 leucocytes)                                                                                       | 27      | 17.5    | 38      | 70      | 20       |
| Erythroblasts (per 100 leucocytes)                                                                                     | 6       | 10.5    | 0       | 9       | 16       |
| White cells/c.mm.                                                                                                      | —       | 18,350  | 42,000  | 47,000  | 25,550   |
| Polymorphs                                                                                                             | —       | 23.5%   | 27%     | 18%     | 28%      |
| Lymphocytes                                                                                                            | —       | 42.5%   | 68%     | 51%     | 49%      |
| Monocytes                                                                                                              | —       | 10%     | 2%      | 18%     | 1%       |
| Eosinophils                                                                                                            | —       | 2%      | 0       | 4%      | 1%       |
| Basophils                                                                                                              | —       | 0       | 1%      | 0       | 1%       |
| Neutrophil myelocytes                                                                                                  | —       | 3.5%    | 1%      | 7%      | 7%       |
| Eosinophil                                                                                                             | —       | 2.5%    | 0       | 2%      | 1%       |
| Basophil                                                                                                               | —       | 0.5%    | 0       | 0       | 0        |
| Metamyelocytes                                                                                                         | —       | 12.5%   | 1%      | 0       | 8%       |
| Myeloblasts                                                                                                            | —       | 3%      | 0       | 0       | 4%       |

TABLE II.—BLOOD CHEMISTRY (PER 100 C.C.)

| Date                                            | 15.6.48 | 10.7.48       | 18.9.48 | 20.10.48 |
|-------------------------------------------------|---------|---------------|---------|----------|
| Acid phosphatase units                          | 3.75    | —             | 1.5     | —        |
| Alk. phosphatase King-Armstrong units           | 18      | 6             | 16      | 11       |
| Serum calcium                                   | 11      | 11.1          | 9.6     | 10.8     |
| Plasma inorganic phosphate (Youngburg's method) | —       | 16 (repeated) | 5       | 3.03     |
| mg. Serum protein total                         | —       | —             | 3.5     | 3.5      |
| Albumin                                         | —       | —             | —       | 1.5      |
| Globulin                                        | —       | —             | —       | 2.0      |
| Blood urea                                      | —       | —             | 48      | 48       |



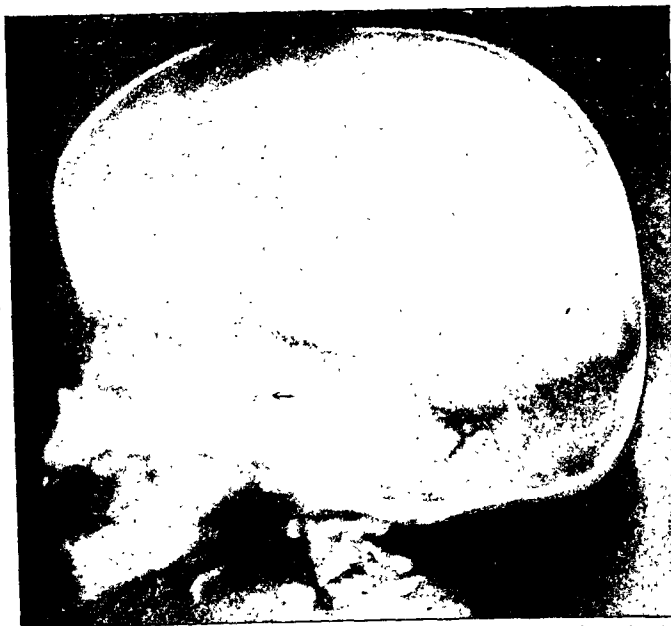


FIG. 1.—Note increased density of base of skull and parietal region with clubbing of posterior clinoids and great narrowing of sella turcica.



FIG. 4.—The humerus is clubbed, especially at the proximal end. The middle of the shaft shows up well the "periosteal encasement".

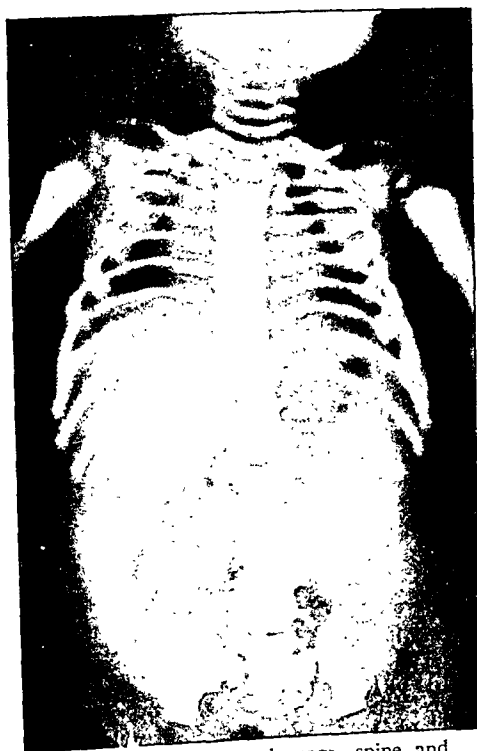


FIG. 2.—The thoracic cage, spine and pelvis show the characteristically increased density.



FIG. 3.—Note clubbing of the ends of the long bones. The periosteal elevations of the shafts and fluffiness of their ends suggest active rickets.

X-rays (Dr. L. G. Blair): The skull is thin with a wide anterior fontanelle and wormian bones posteriorly (fig. 1). The bones of the limbs are slender and show possibly thinning of the cortices and coarsening of trabeculation (fig. 2). This is more marked in the legs than in the arms.

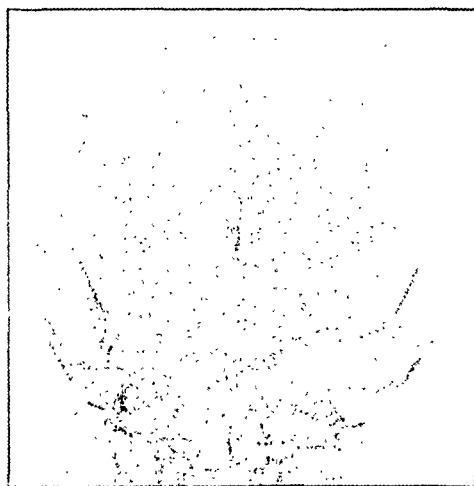
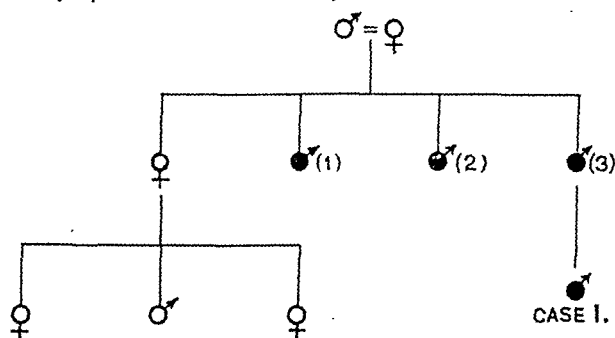


FIG. 1 (Case I).—Showing wide fontanelle and wormian bones.

*Progress.*—Height 31½ in., weight 22 lb. 14 oz. at 1 year 10 months.

The boy can now stand with support. The muscle tone appears normal, but there is still some laxity of ligaments. He now has 16 apparently normal teeth. The anterior fontanelle is still widely open. There is no history of fractures.



♂=Normal Male. ♂=Abnormal Male. ♀=Normal Female.

Family tree of Case I.

(1) Blue sclerotics. 74 in. in height. No history of fractures.

(2) Died at about 40 years old. Was dwarfed and had had about five fractures of the femora from comparatively minor injuries. The first fracture occurred at 1 year of age.

(3) Father of Case I now aged 46. Had first fracture at 3 months of age. He has had about 24 fractures, nearly all of the femora. The last fracture occurred eleven years ago. His height is 54½ in. The sclerotics are faintly blue. There is gross deformity of both thighs and some bowing of the legs. X-rays (Dr. L. G. Blair): There is considerable bowing of the tibia and fibula on both sides and coarsening of trabeculation. The changes are more marked in the upper ends of the femora, where there is considerable varus deformity. The bony structure of the pelvis shows considerable changes. There have been old fractures of the femora (fig. 3).

The other members of the family are reported to be normal, but none, other than the father of Case I, has been examined by us. No history of otosclerosis. On the mother's side there is no relevant family history.

## TABLE III.—URINE INORGANIC PHOSPHATES

|          |                                                        |
|----------|--------------------------------------------------------|
| 10.7.48. | 125 mg./100 c.c. (when the plasma was 16 mg./100 c.c.) |
| 18.9.48. | 952 mg./100 c.c. (when the plasma was 5 mg./100 c.c.)  |

*Treatment.*—Intramuscular penicillin failed to affect the snuffles, but local penicillin instillations cleared up the conjunctivitis. Adexolin minims 10 t.d.s. and ferri et ammon. cit. grains 5 t.d.s. were given from June 17 for six weeks.

*Progress.*—During the month following admission, the spleen enlarged to 3 fingers. Head circumference  $18\frac{1}{2}$  in. Developed whooping cough on 26.7.48 and was transferred to an isolation hospital where she contracted a severe gastro-enteritis. On readmission on 18.9.48 she was found to have bilateral conjunctival hæmorrhages, head circumference  $18\frac{1}{2}$  in., liver no larger than before, spleen now 4 fingers. A month later, the head circumference was  $18\frac{1}{2}$  in.

*Comment.*—Albers-Schönberg disease is rare, 148 cases having been described up to the end of 1946 (Pines and Lederer, 1947). It is usually diagnosed by X-ray following a fracture, but in infancy, with little opportunity for bony injury, it may be recognized by the features illustrated in this case. This patient, however, presents some points of particular interest: First, a familial incidence has not been established and the parents are not consanguineous. Blood relationship between the parents has been stated by Nussey (1938) to be present in the malignant type of this disease, of which this is undoubtedly an example. Secondly, it is surprising that this infant survived whooping cough and gastro-enteritis. Thirdly, the blood chemistry is peculiar in that the plasma inorganic phosphorus was 16 mg., whereas the highest figure so far recorded is 7 mg. per 100 c.c. Two months later, however, a fall is noticed with a greatly increased output of inorganic phosphates in the urine. No acceptable explanation can be produced for the high level of plasma phosphorus obtained but it is at least theoretically possible that this may have stimulated the parathyroid glands to produce the subsequent fall in the blood through increased excretion in the urine. It is known that the parathyroids can stimulate an osteoclastic reaction for the resorption of bone. This would be followed by a wave of osteoblastic deposition of new bone since, according to Zawisch (1947), resorption and deposition are two phases of bone formation which condition and stimulate one another. Parathyroid activity may therefore be associated with attempts at repair but unfortunately injections of this hormone have hitherto proved valueless.

Some light has been thrown on this disease by the careful histological work of Zawisch who has produced evidence to show that it begins *in utero* at the second period of development of bone formation which, in the case of the femur, is about the fifth month of intra-uterine life. Most authorities believe that the disorder is probably due to damage to the undifferentiated mesenchyme which, being the progenitor of both the hæmopoietic and osseous systems, would give rise to the bone and blood pictures characteristic of this disease.

## REFERENCES

- NUSSEY, A. M. (1938) *Arch. Dis. Childh.*, 13, 161.  
 PINES, B., and LEDERER, M. (1947) *Amer. J. Path.*, 23, 755.  
 ZAWISCH, C. (1947) *Arch. Path.*, 43, 55.

**Osteogenesis Imperfecta Presenting With Delay In Walking (Two Cases).**—J. P. M. TIZARD, M.R.C.P. (for W. G. WYLLIE, M.D., F.R.C.P., and BERNARD SCHLESINGER, O.B.E., M.D., F.R.C.P.).

CASE I.—Boy aged 1 year 10 months.

Brought to hospital at 1 year 4 months of age on account of delay in walking.

*History.*—Only child. Normal delivery at full term. Birth-weight 7 lb. 11 oz. Both anterior and posterior fontanelles patent and wider than usual. Right arm swollen and reddened, but X-ray showed no fracture. Breast fed for six weeks. Then developed pyloric stenosis, which was treated operatively.

*Milestones.*—Held up head at 4 to 5 months. Sat unsupported at 10 months. Began to stand with support at 20 months. In other respects has not appeared backward.

*Examination* at 16 months. A healthy-looking child. Weight 20 lb. 9½ oz. Large, rather square head with parietal prominences. Skull circumference 19½ in. Anterior fontanelle about 2 in. in coronal line. Scleræ faintly blue (within normal limits). 11 teeth. Slight muscular hypotonia and slight hyper-extensibility at large joints. Tendon reflexes normal. No sign of rickets. Other systems normal.

*Investigations.*—Blood chemistry (Dr. W. W. Payne). Inorganic blood phosphorus 4.3 mg. per 100 c.c. Alkaline plasma phosphatase 20.2 units (10–20). Serum calcium 10.6 mg. per 100 c.c.

Tuberculin tests negative.

muscles in the limbs and the erector spinæ show normal excitability. There is no sign of a sluggish or delayed response to stimulation. Relaxation after contraction is perhaps slightly more rapid and complete than normal. (3) There is no evidence of any myotonia.

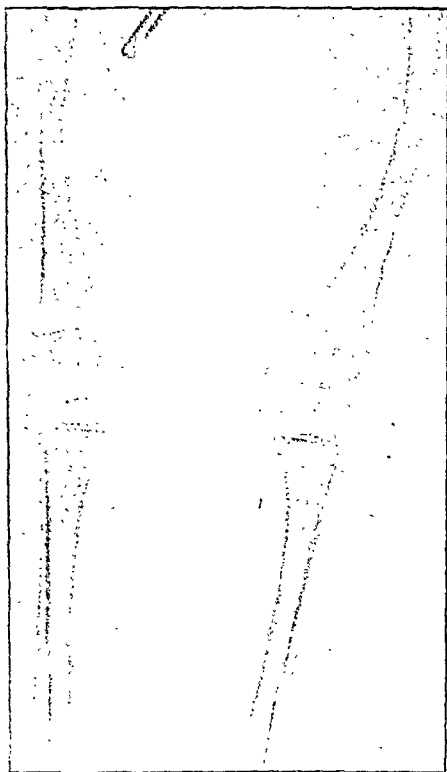


FIG. 4 (Case II).—See text.

*Comment.*—Cases of osteogenesis imperfecta are usually reported as presenting with fractures. In neither of these cases was this so, both children being brought to hospital on account of delay in walking. Both children were found to have laxity of ligaments which is often present in osteogenesis imperfecta and it is suggested that the apparent delay in motor development was due to difficulty in fixation of joints.

Ottley, quoting Larat and Bolton, mentions abnormal electrical muscle reactions in cases of osteogenesis imperfecta. In these two cases there was slight hypotonia on clinical examination, probably the result rather than the cause of the delay in motor development, but the electrical muscle reactions were normal.

The family history of Case I is also of interest. It suggests that a mutation must have taken place in a generation prior to that of the father's, although both grandparents are said to have been normal.

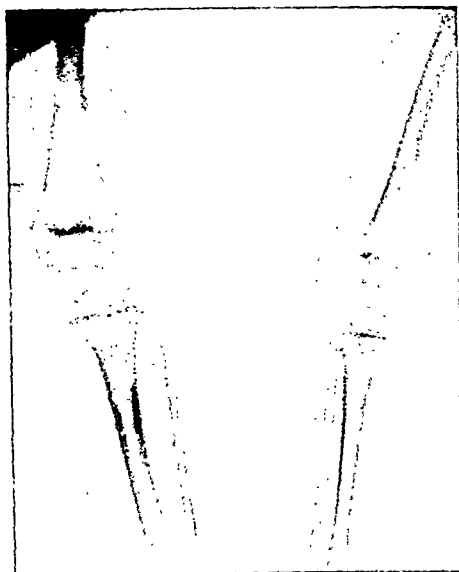
#### REFERENCE

OTTLEY, C. M. (1932) *Arch. Dis. Childh.*, 7, 137.

**Acute Infective Polyneuritis.**—HUGH R. JOLLY, M.R.C.P. (for WILFRID SHELDON, M.D., F.R.C.P.).

Boy aged 8 years.

*History.*—Perfectly well until June 1948 when he began to complain of weakness of the left leg and a vague ache in the back and left hip. He staggered on walking and fell repeatedly. Three weeks later the weakness had increased so that in order to rise after falling he had to "climb up his legs." No history of suspicious contact.



CONTROL

FIG. 2 (Case I).—Right leg with normal control (one month older).

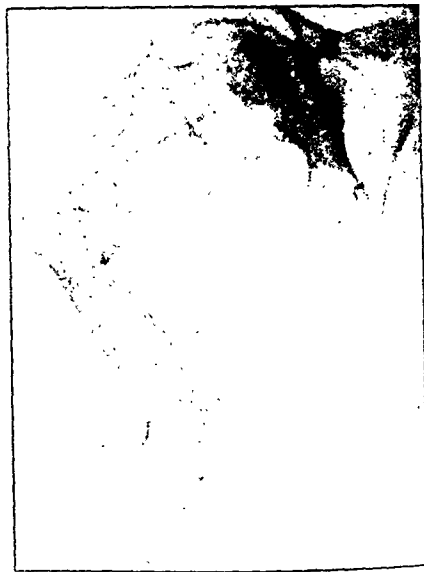


FIG. 3.—Father of Case I. Left femur.

**Muscle reactions** (Dr. A. K. Tyler).—The electrical reactions are as follows: (1) Nerve conduction is present. The nerve chronaxie is within normal limits. (2) The peronei, quadriceps, extensor femoris, hamstrings, erector spinae and forearm flexors and extensors show normal excitability. There is no sign of any sluggish or delayed response to stimulation. Relaxation after contraction is slightly more rapid and complete than normal. (3) No evidence of myotonia is present.

**CASE II.**—Girl aged 2 years 1 month.

**History.**—Brought to hospital at 1 year and 10 months on account of delay in walking. The previous two pregnancies had resulted in miscarriages at the seventh month. Normal delivery at full term. Birth-weight 8 lb. Bottle fed. Normal vitamin supplements. No family history of fragile bones, blue sclerotics or otosclerosis. One younger and four older siblings are normal.

**Milestones.**—Sat up at 12 months. Stood with support at 1 year 11 months. Has not appeared backward in other respects. Has always appeared "double jointed" and sleeps with her feet round her ears.

**Examination.**—At 1 year 10 months. A healthy-looking child. Weight 20 lb. 8 oz. Apparently normal intelligence. Square skull with prominence over the ears. Circumference 19½ in. Anterior fontanelle widely open. Sclera slightly blue (probably within normal limits). Slight generalized hypotonia especially of lower limbs. Marked laxity of ligaments. Tendon reflexes normal. Other systems normal. No evidence of rickets.

**Investigations.**—Blood chemistry (Dr. W. W. Payne). Inorganic blood phosphorus 3.5 mg. per 100 c.c. Serum calcium 9.4 mg. per 100 c.c. Alkaline plasma phosphatase 18.3 units (10–20).

**X-rays** (Dr. L. G. Blair): Bones of skull are thin and there is increase in the inter-parietal diameter. There are some wormian bones posteriorly. The fontanelle is still present. The bones of the limbs are slender and there is possibly thinning of the cortices and coarsening of trabeculae. This is more marked in the legs than in the arms. The femora are bowed and there have probably been old subperiosteal fractures (fig. 4).

**Progress.**—At 2 years 1 month she cannot yet walk. Crawls and climbs stairs. Height 31 in. Fontanelle still 1½ in. open in coronal line. 20 teeth which appear translucent and decalcified. Muscle tone appears normal, but there is still some hyperextensibility of joints. No history of fractures.

**Electrical reactions** (Dr. A. K. Tyler).—The electrical reactions of the muscles are as follows: (1) Nerve conduction is present. The nerve chronaxie is normal. (2) Representative

## Adrenalin Test

|                            | Before |    | 5 m Adrenalin<br>(1/1000)<br>I.M. | After |    |    |    |    |    |    |    |
|----------------------------|--------|----|-----------------------------------|-------|----|----|----|----|----|----|----|
|                            | 50     | 49 |                                   | 66    | 51 | 52 | 54 | 61 | 60 | 59 | 56 |
| Blood sugar in mg./100 ml. | 50     | 49 |                                   | 66    | 51 | 52 | 54 | 61 | 60 | 59 | 56 |
| Time (minutes) .. ..       | -10    | -5 | 0                                 | 10    | 15 | 20 | 35 | 50 | 65 | 80 | 90 |

## Galactose Tolerance Test (40 grammes of galactose given by mouth)

|                                |         |        |        |          |         |
|--------------------------------|---------|--------|--------|----------|---------|
| Blood galactose in mg./100 ml. | 0       | 21     | 28     | 21       | 21      |
| Time .. .. .                   | Fasting | ½ hour | 1 hour | 1½ hours | 2 hours |

Blood glycogen 19 mg./100 ml.

Plasma cholesterol 282 mg./100 ml.

Total plasma proteins 7.3 grammes/100 ml.; albumin 4.0 grammes/100 ml.; globulin 2.96 grammes/100 ml.; fibrin 0.34 gramme/100 ml.; A/G ratio 1.35 : 1.

Serum inorganic phosphate (fasting) 4.7 mg.%. Serum potassium (fasting) 20.6 mg.%. Stool: No excess of fats; no starch; no meat fibres.

W.R. negative.

Blood picture.—Hb 80%. Red cells show moderate anisocytosis and slight anisochromia. Reticulocytes less than 1%. Total W.B.C. 7,100 per c.mm. (P. 55%, E. 2%, L. 41%, M. 2%). Platelets 180,000/c.mm. Clotting time 1 min. 37 secs. Bleeding time 4 mins 26 secs.

X-rays of heart, lungs, skull and carpus normal. E.C.G. normal.

**Sarcoidosis.**—MEGAN P. JONES, M.B., D.C.H. (for URSULA JAMES, M.R.C.P.).

N.B., male, aged 9 years.

**History.**—For four months he had repeatedly been excluded from school because of "mumps". There were no other complaints and the past and family histories were not significant.

**On examination.**—Slightly undersized and underweight. Very poor posture. Persistent evening temperature of 99° F. Bilateral, symmetrical, non-tender enlargement of the parotids. General enlargement of peripheral lymph glands (neck, axillæ, groins, epitrochlears). Moderate enlargement of liver and spleen.

Mantoux 1/1000 negative. W.B.C. 9,500/c.mm. (polys. 73%, lymphos. 9%, eosinos. 11%, monos. 7%). Serum calcium 14 mg./100 ml. Serum proteins total 8.3 grammes/100 ml., albumin 4.7 grammes/100 ml., globulin 3.6 grammes/100 ml. E.S.R. 10 mm./hr. X-ray chest and bones normal. Lymph gland biopsy—histological picture of sarcoidosis.

**Comment.**—Sarcoidosis has been relatively rarely reported in childhood. Indeed only 22 cases under the age of 10 could be traced. Parotid involvement in childhood has only been noted twice before.

**Fersolate Poisoning.**—R. C. ROXBURGH, M.B. (for CHARLES F. HARRIS, M.D., F.R.C.P.).

Boy aged 16 months.

**History.**—On 8.10.48, at 11 a.m., swallowed approximately 50 tablets "Fersolate" and shortly afterwards, an unknown quantity of mist. magnes. trisilic. Immediately vomited approximately 20 tablets. Taken to nearest hospital, where stomach was washed out. Admitted to Westminster Children's Hospital 1.30 p.m.

**On admission.**—T. 98° F., P. 150, R. 25; appeared rather drowsy, but colour good. Lips and neck were stained yellowish-brown colour by vomitus. A strong smell of iron was noticed. Pupils reacted to light briskly. Tongue and fauces were stained a deep brown. Heart and lungs N.A.D. Abdomen: no tenderness, liver edge just palpable, firm, one fingerbreadth below costal margin.

**Treatment.**—Stomach washout was returned a deep pink colour (chemical examination showed hæmoglobin in solution). Given ½ oz. mag. sulph. by mouth, liberal fluids, mist. pot. cit. Penicillin I.M. 200,000 units daily as prophylactic measure. B.A.L. 0.3 c.c. given b.d. for three days, I.M. injections.

**Course.**—Four hours later began passing fluid black motions, mixed with blood and mucus, continued for twelve hours, 6 stools in all. Urine: deep orange-brown colour, no albumin, no blood found, but gave orange reduction to Benedict's solution.

9.10.48: Remained rather drowsy and irritable, vomited four times. T. 99.8° F., P. 150; stools were black and semiformal, not obviously blood-stained. Urine brownish orange

**Examination.**—Very bright boy. Temperature 99° F. Pulse 100. Slight nystagmus on lateral deviation to left. Marked weakness of back muscles and of all the muscles of the legs, this being a little more so on the left.

All superficial reflexes absent in upper and lower limbs. Sensation normal except for slight diminution of vibration sense at the extremities.

Walks with an ataxic gait on a wide base and in order to rise from lying down, rolls on to his stomach and climbs up his legs.

**Investigations.**—C.S.F. (20.7.48): Clear colourless fluid. 1 cell per c.mm. Protein 180 mg.%. Blood: W.B.C. 5,500. No anaemia. No punctate basophilia.

X-rays of long bones: No evidence of lead poisoning. Schick test negative (previously immunized). Throat swab: No diphtheria bacilli.

**Progress.**—For the first three weeks in hospital the weakness in the legs increased so that he was finally unable to raise them against gravity, and in addition, weakness of the hands appeared. He also became unable to walk unaided and could no longer raise himself from the ground.

Since this time he has made a gradual but progressive improvement, vibration sense has returned, nystagmus has disappeared, and although the muscle weakness is still severe, he can now walk on his own and get up off the ground.

C.S.F. (8.10.48): 1 cell per c.mm., protein 220 mg.%.

**Comment.**—The interest in this case lies principally in its similarity to pseudo-hypertrophic muscular dystrophy, a diagnosis which was ruled out by the finding of the high protein content of the cerebrospinal fluid.

### Hepatic Glycogen Disease.—L. G. SCOTT, M.B. (for P. R. EVANS, M.D., F.R.C.P.).

H. B., male aged 11 years.

Had large abdomen since 3 months old.

**Family history.**—Parents healthy, not related. Two brothers (14 and 17) well. Eldest brother had Von Gierke's disease and died of cerebral malaria aged 2 years. Paternal grandmother and her son had "kidney trouble". Nil else relevant.

**Previous illness.**—Had malaria three or four times (type unknown). Nil else relevant.

**History.**—Normal birth and milestones, except slightly late in walking (2 years), and cutting teeth (9 months). Born in Rhodesia and has been at school there since 7 years old. Said to be two years backward at school.

**Present illness.**—Distension of abdomen noticed at 3 months. In hospital from 10 months old to 17 months with otitis media, and became very fat. Fatness tended to go when he walked at 2 years. Mother thinks abdominal distension has decreased since aged 4 years. Mother noticed breath smelt sweet from about 3 months old until two years ago. Used to vomit frequently, usually in mornings, but hardly ever now unless tired or after dietary indiscretion. Micturition normal. Enuresis up to 8 years old. No faintness, headaches, or convulsions. Always had slight breathlessness on exertion and gets "stitch" easily. No more liable to infections than other children.

**On examination.**—Plump, happy, and intelligent boy with a distended abdomen. Superficial veins prominent over chest, abdomen and back.

Weight 70 lb. 8 oz. (normal average 72 lb.); height 51 in. (normal average 54 in.); Chest 27½–28 in. Mouth, throat, and ears satisfactory. No lymphadenopathy. Heart N.A.D. B.P. 120/85. Pulse 100 regular.

Exercise tolerance test (20 times on and off chair) 100: 164: 128: 130; slight dyspnoea. Chest N.A.D.

Abdomen: Liver greatly enlarged, extending from fourth intercostal space in right axillar line to 6 in. below costal margin at lowest point. Firm and smooth. Spleen and kidneys not palpable. Testicles not in the scrotum, but the left one can be brought down, the right one is in the inguinal canal, and both seem normal. C.N.S.: N.A.D.

The urine contained a trace of acetone on only one occasion. About ten early morning specimens were examined by Rothera's and the ferric chloride tests.

**Investigations.**—Blood sugar 118 mg./100 ml. (Folin and Wu.)

Glucose tolerance test (Capillary blood sugar—Shaffer-Hartmann method; 35 gramm of glucose given orally):

|                           |         |        |         |
|---------------------------|---------|--------|---------|
| Blood sugar (mg./100 ml.) | 36      | 57     | 102     |
| Time                      | Fasting | 1 hour | 2 hours |

100 grammes. Twenty-four-hour excretion: 26.5 and 9.6 mg. urobilinogen on two estimations.

*Blood*.—Hb 64%; R.B.C. 4,000,000. W.B.C. 9,500; normal differential. Reticulocytes 1.2%. Platelets 266,000. Fragility normal. Bleeding time seven minutes four seconds. Coagulation time four minutes fourteen seconds. van den Bergh: Direct reaction 4.5 mg. Alkaline phosphatase 36 units. Plasma protein 6.3 grammes. Albumin 4.1; Globulin 2.2 grammes/100 c.c. Cholesterol 1,200 mg./100 c.c. W.R. negative. Blood urea 83 mg./100 c.c.

Mother's blood Rhesus positive, child's Rhesus negative.

Blood cholesterol of mother and one sister within normal limits.

X-rays of skull, chest and long bones revealed no abnormality.

*Treatment*.—Low cholesterol diet and thyroid extract,  $\frac{3}{4}$  grain a day for three weeks, without clinical improvement.

**Pulmonary Hæmosiderosis.**—ALISON B. KING, M.B. (for MARY WILMERS, M.D.).

O. R., female, aged 2 years 8 months.

*Family history*.—Negative.

*History*.—Well until mild attack of measles in May 1948, after which child became lethargic, pale, constantly tired and breathless after little exertion. Appetite poor and weight static. Began to get repeated coughs and colds. Two attacks of "bronchitis" in June and September each lasting a week. Child was very ill with cough, fever and vomiting. There was no cyanosis. After June attack, jaundiced. Urine said to be darker than usual, after attack. Stools not pale. After July, urine and stools normal.

*Examination*.—Very pale, alert child. Normal height and weight for age. No physical signs in heart or lungs. Blood-pressure 106/70. Abdomen: Spleen not palpable. Liver palpable  $\frac{3}{4}$  in. to 1 in. below costal margin.

*Progress*.—Two hæmatemeses. 7.10.48: Occult blood in stool.

*Investigations*.—7.7.48: Hb 50%. C.I. 1.0. E.S.R. 4 mm/hr. Reticulocytes 2%. 8.8.48: Hb 78% (on iron therapy). 5.10.48: Hb 50%—after September attack of "bronchitis". C.I. 0.8. Reticulocytes 3%. 15.10.48: Hb 72% (on iron). 7.7.48: W.B.C. 8,600/c.mm. Normal differential. Urobilinogen not increased. Fragility of R.B.C., serum bilirubin, platelets, normal. W.R. and Mantoux 1:1,000 negative.

X-ray chest: Diffuse pulmonary shadowing resembling œdema or ecchymosis—would fit the descriptions of hæmosiderosis of the lung.

*Diagnosis*.—Hæmosiderin-laden phagocytes found in material from lung puncture, stomach washings and sputum.

**Multiple Aneurysms (? Congenital).**—D. A. J. WILLIAMSON, M.D., M.R.C.P. (for BERNARD SCHLESINGER, O.B.E., M.D., F.R.C.P.).

Girl aged 9 months.

*History*.—Well until June 1948 when admitted to a hospital with otitis media and meningitis. C.S.F. contained increase in W.B.C. but no organisms cultured. Treated with sulphamezathine and systemic and intrathecal penicillin with complete recovery.

July: Boil in right thigh.

9.8.48: Lumps noticed in axillæ while bathing.

12.8.48: Sudden onset of vomiting and limpness.

13.8.48: Noticed to have complete flaccid left hemiplegia. No loss of consciousness but failed to recognize parents.

Admitted to hospital again. C.S.F. was normal except for the presence of 300 R.B.C. per c.mm. which were thought to be traumatic. The hemiplegia later became spastic but less marked.

1.10.48: Developed crop of petechiæ on left arm and leg.

*Examination*.—Intelligent contented baby.

C.N.S.: Reduced movements of left side of face and of left arm and leg. Early trophic change of left hand and foot. Head and eyes tend to be turned to right. Tone—some



colour, no albumin or blood found. Centrifuged deposit: W.B.C. 2-3, R.B.C. occasional, no casts or crystals.

Blood count: Hb 89%; R.B.C. 4.6 million; W.B.C. 14,000.

During the next four days he improved slowly, and there was no further diarrhoea or vomiting. Had evening temperature 100.6° F., pulse remained at 140 to 160. Hæmoglobin dropped to 72%. Prothrombin time 20 sec.

Urine iron estimation: (12.10.48) 0.5 mg.%; (13.10.48) 0.1 mg. %.

Urine bile (12.10.48): Bile salts and urobilinogen present, bilirubin absent.

*Liver function tests* (14.10.48):

|                 |          |    |           |                       |            |
|-----------------|----------|----|-----------|-----------------------|------------|
| Serum bilirubin | Direct   | .. | 0.1 mg. % | Serum cholesterol     | 147 mg. %. |
|                 | Indirect | .. | 0.1 mg. % | Thymol turbidity test | 1 unit.    |
|                 | Total    |    | 0.2 mg. % | Thymol flocc. test    | negative.  |

Serum alk. phosphatase 12 units.

Serum colloidal gold negative.

By 15.10.48 the child had recovered clinically.

**Calcified Intrathoracic Tumour in an Infant.** ? Dermoid Cyst.—J. DEAN, M.R.C.P. (for IAN M. ANDERSON, M.D.).

W. C., male, aged 13 months.

*History.*—Well up to age of 4 months. Since then four mild attacks of "bronchitis". At age of 10 months developed cough, pyrexia, dyspnoea and cyanosis.

*On examination.*—Extensive dullness to percussion and diminished air-entry at right base posteriorly.

X-ray: Large calcified cyst-like opacity in the right thoracic cavity with collapsed or consolidated lung around the anterior margin.

*Progress.*—The pneumonic process subsided in six days and he has subsequently been quite well.

*Investigations.*—Mantoux 1/100 negative. Casoni test negative. Blood-count: W.B.C. 9,000 (P. 36%, L. 58%, M. 4%, E. 2%).

X-ray of chest: "Large extrapulmonary tumour or cyst with linear calcification at the periphery and punctate calcification elsewhere. Bone absorption in the posterior border of the right rib—this looks old. Heart and œsophagus displaced to the left. Spine normal. If the child were older I would say this was an inspissated tuberculous empyema" (Dr. Peter Kerley).

**Xanthomatosis.**—P. M. SMYTHE, M.R.C.P. (for R. H. DOBBS, M.D., F.R.C.P.).

Girl, aged 2½ years.

*Family history.*—Father alive and well. Mother had toxæmia with both pregnancies. One sister aged 4½, alive and well.

*Personal history.*—Normal labour, birth-weight 6½ lb. ? jaundiced at birth. Definitely jaundiced when 2 days old, and has remained so; jaundice fluctuating in intensity. No vomiting.

Aged 20 months: Yellow eruptions appeared in the skin and pruritis, always present, became more marked. Diet had been fat free.

*On examination.*—Weight 21 lb. Height 32 in. Extensive xanthomatous tuberose deposits in skin, especially over the elbows, ankles and knuckles. Miliary deposits in the palms, left thigh, and soles of feet. Streaks along skin creases, also in gum margins. Teeth slightly green, some carious and loose.

C.V.S.: Systolic murmur, loudest in the aortic area. B.P. 100 mm. Hg systolic.

Abdomen: Liver and spleen enlarged 1 in.

C.N.S.: Mentally backward. Unable to stand. Fontanelle still open. Fundi: Left disc ? blurred. Voice at times gruff and harsh. Knee- and ankle-jerks absent.

Laryngoscopy: One small pin-head yellow patch on left arytenoid ? xanthoma. Left vocal cord moving less freely than the right.

*Investigations.*—Urine: Urobilin and urobilinogen within normal limits. Bile and albumin: a trace.

Fæces: Colour varies from grey to light brown. Fæcal urobilinogen; 14 and 53 mg. per

## Section of Orthopædics

President—H. J. SEDDON, M.A., D.M., F.R.C.S.

[October 5, 1948]

**Infective Arthritis of the Left Hip-Joint.**—W. E. TUCKER, F.R.C.S.

B. S., aged 12 years.

24.11.46: Patient admitted to the London Homœopathic Hospital. Three days before admission she had slight pain in the left groin. A few hours later the pain had increased in severity, and she had to lie down. There was no previous history of injury to the left hip-joint. The pain was aggravated by movement, and was localized to the middle of the left groin, and down the middle of the left thigh for about 3 in. On admission the patient was running a hectic temperature, and was gravely ill.

There was incontinence of fæces and urine. On inspection nothing abnormal could be seen. On palpation there was no swelling or tenderness. Movements: Flexion was markedly limited and painful, as well as rotations and adduction, but abduction was free and painless. The other systems were normal.

She was put on penicillin 50,000 units three-hourly. Blood-count on 27.11.46: W.B.C. 7,800 per c.mm. (polys. 66%, lymphos. 33%, large monos. 1%).

Aspiration of the joint was carried out without obtaining any fluid, and the hip was encased in a plaster spica with skin traction.

X-rays taken at this stage were reported to show no evidence of osteomyelitis. The general condition of the patient improved, but the temperature never settled completely. Towards the end of December 1946 there was a recurrence of pain, and a sharp rise in temperature.

On 16.12.46 the white cell count was 9,200 c.mm. (polys. 63%, lymphos. 36%, large monos. 1%). The B.S.R. was 130 in the first hour, and 140 in the second.

On 1.1.47 under general anæsthesia a needle was inserted into the joint and pus evacuated. Exploration of the greater trochanter was carried out, and the neck of the femur drilled. Large quantities of pus were evacuated. Penicillin cream was applied locally to the joint, and a further course of penicillin started. *Staphylococcus aureus* was isolated from the pus, and this was found to be penicillin-sensitive.

On 27.1.47 R.B.C. 3,500,000 per c.mm.; C.I. 0.9%; W.B.C. 15,000 (polys. 80%, lymphos. 20%).

FEB.—ORTHOP. 1

spasticity of left arm and leg. Tendon reflexes increased on left with extensor plantar response. Fundi normal.

Skull: Circumference 17½ in. No vascular hum audible.

Cardiovascular system: Heart not enlarged. Sounds normal. B.P. 125 systolic, in both arms. Three aneurysms palpable: (1) L. axillary artery about 1 in. in diameter; (2) R. axillary artery about ½ in. in diameter; (3) R. femoral artery about ½ in. in diameter.

*Investigations.*—*Blood:* Hb 91%; R.B.C. 4.51 million; W.B.C. 11,500 (P. 68%). B.S.R. 14 mm. in one hour. C.S.F. normal. Urine: N.A.D. W.R. and Kahn negative.

X-ray skull and chest N.A.D. E.C.G.: N.A.D. Right-sided carotid angiogram unsuccessful.

*Comments.*—It is thought that the aneurysms are congenital in origin. Mycotic aneurysms are unlikely in the absence of bacterial endocarditis. Syphilis is excluded by the serological tests and the lack of other evidence of the disease. Congenital aneurysms of major peripheral vessels are extremely rare and do not usually present until adult life when they are most often found at flexures, e.g. on the popliteal or axillary arteries.

It is considered that the hemiplegia is probably due to a further aneurysm situated on one of the intracranial arteries, perhaps the right middle cerebral.

Dr. J. R. D. Webb's case of Polyostotic Fibrous Dysplasia, shown at this meeting, will be reported in the next issue of the *Proceedings*, Section of Paediatrics.



FIG. 1A.

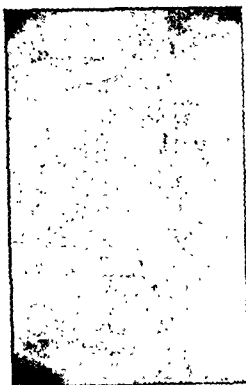


FIG. 1B.



FIG. 2A.



FIG. 2B.



FIG. 3A.



FIG. 3B.

FIGS. 1A and 1B.—These original X-rays (taken 9.1.48) show the compression erosions on which the provisional diagnosis of tubercle was first made.

FIGS. 2A and 2B.—Taken five weeks later, showing almost complete destruction of the affected vertebra, and doubtful marginal erosion of the vertebra below. The condition is probably that rare type of tubercle, a diffuse osteitis, and the rapidity of collapse due to continued weight-bearing.

FIGS. 3A and 3B.—Taken seven months later (27.9.48) after immobilization on a frame, showing correction of deformity and definite reactive bone formation.

the vertebra was thought due to the fact that he remained ambulant in the early stages of the disease.

*Subsequent progress.*—He has been immobilized on an abduction frame at St. Vincent's Hospital since March. His general condition has improved tremendously. He has no pain and his paraplegia has recovered completely. His X-rays (27.9.48) (figs. 3A and 3B) reveal much new bone formation.

He developed a lumbar abscess at the end of August. It increased in size despite aspiration and was opened and evacuated on September 30 and primary suture effected.

(I wish to thank Mr. E. P. Brockman for permission to publish this interesting and instructive case.)

By the end of January patient's general condition was improved. Penicillin was stopped. On 18.2.47 plaster was removed, and skin traction applied to both legs.



FIG. 1.—Infective arthritis of left hip with subluxation, showing destruction of the upper segment of head of left femur.

On 24.2.47 white cell count showed 12,180 per c.mm. (polys. 77%, lymphos. 23%).

The wound had now healed, and she was started on bed exercises and faradism.

X-rays taken on 11.8.47 showed considerable increase in the destruction of the femoral head and neck (fig. 1). A couple of small sequestra were present in the area of the femoral head.

Patient has gradually improved, and has been allowed out on a walking caliper. There is shortening of the left leg  $\frac{3}{4}$  in., and the movements now show 5 degrees of fixed flexion. Flexion is possible to 60°. Rotation is markedly limited. Abduction is nil.

POSTSCRIPT.—The case was shown for discussion as to further treatment. 400,000 units of penicillin were given daily for three weeks but it is realized that this, according to present estimates, is only a small dose.

### Tuberculous Disease of the Spine Simulating Malignancy in a Male Patient aged 30.— P. I. HYWEL-DAVIES, F.R.C.S.

*History.*—He first complained of the acute onset of lumbar pain (with associated night sweats) in November 1947 and was treated in bed by his own doctor (as lumbago) for a fortnight. He improved, but after restarting work after Christmas, the pain reappeared.

He was then seen at Acton Hospital and tubercle diagnosed on the clinical findings of local tenderness and bilateral psoas spasm, and the X-ray appearances (9.1.48) (figs. 1A and 1B). His name was placed on the waiting list for admission to St. Vincent's Orthopaedic Hospital and he returned home. He did not remain completely in bed and became progressively worse—a month later he became unable to walk owing to complete loss of use of the right lower limb.

An X-ray taken then (16.2.48) (figs. 2A and 2B) showed such rapid destruction of the diseased vertebra that malignancy was now considered. He was admitted to Acton Hospital and remained under observation for three weeks; thorough investigation as to a possible primary focus proved negative.

He was transferred to Westminster Hospital where he remained under observation a further week.

*Examination* revealed a marked angular kyphus in the upper lumbar region with associated scoliosis and much muscle spasm. He had a flaccid paresis of the right lower limb and diminished reflexes in the left. Patchy anæsthesia was present over the outer aspect of the right thigh and leg. There was no loss of sphincter control. His pain had diminished and was of the nature of a dull ache.

It was considered that tubercle was the most probable diagnosis because of the diminution of pain with absolute bed rest, coupled with the fact that secondary deposits do not commonly give rise to a flaccid paresis. The marked destruction of



FIG. 1A.

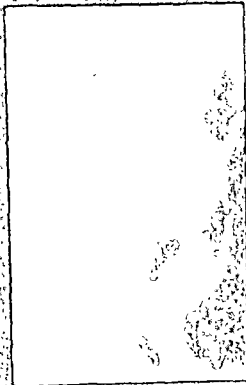


FIG. 1B.

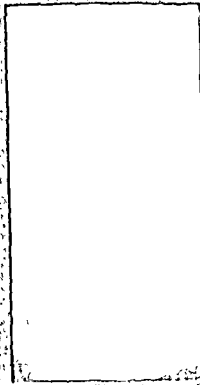


FIG. 2A.

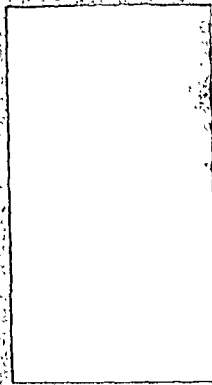


FIG. 2B.

FIGS. 1A and 1B.—These original X-rays (taken 9.1.40) show the compression fractures on which the provisional diagnosis of tubercle was first made.

FIGS. 2A and 2B.—Taken five weeks later, showing almost complete destruction of the affected vertebra, and doubtful marginal erosion of the vertebra below. This condition is probably that rare type of tubercle, a diffuse osteitis, and the rapidity of collapse due to continued weight-bearing.

FIGS. 3A and 3B.—Taken seven months later (27.9.40) after immobilization on a frame, showing correction of deformity and definite reactive bone formation.

FIG. 3A.

FIG. 3B.

vertebra was thought due to the fact that he remained ambulant in the early stages of the disease.

*Subsequent progress.*—He has been immobilized on an abduction frame at Vincent's Hospital since March. His general condition has improved tremendously. He has no pain and his paraplegia has recovered completely. His X-rays (Figs. 3A and 3B) reveal much new bone formation.

He developed a lumbar abscess at the end of August. It increased in size despite treatment and was opened and evacuated on September 30 and primary sutured.

Two Cases by G. P. ARDEN, F.R.C.S.

### I. Polyostotic Fibrous Dysplasia.

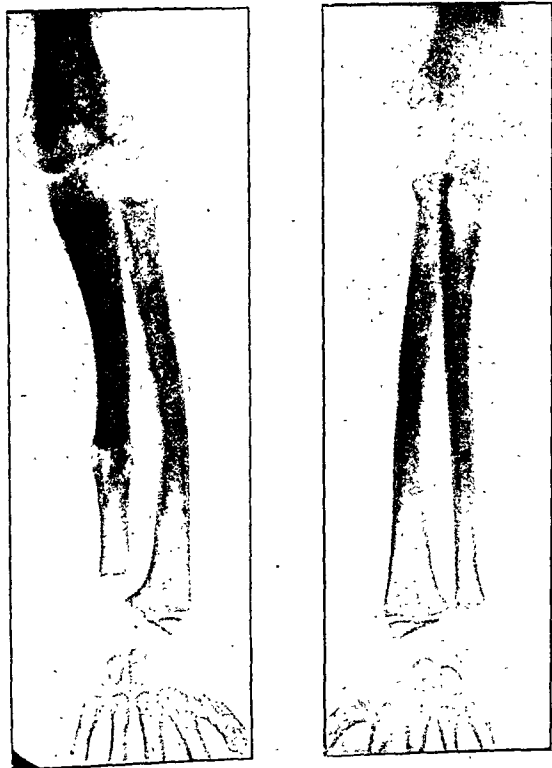
A boy, aged 6, complaining of a vague ache in the right hip and difficulty in walking.

*Family history.*—Rest of family normal.

*On examination.*—Bony swelling in region of left frontal bone, with orbit displaced downwards. Lower end of left ulna absent. While in hospital ran a mild pyrexia up to  $99.4^{\circ}$  F. several times, and  $101.4^{\circ}$  F. once.



(Case I) FIG. 1.



(Case I) FIG. 2.

X-rays show a cystic area involving the right upper femur. several areas in shaft of left ulna, while the lower end of the ulna is absent (figs. 1 and 2). Small areas affecting both humeri and new bone formation affecting the left frontal area of the skull. The left frontal sinus is obliterated and the left orbit displaced downwards.

*Investigations.*—Serum phosphorus  $4.6$  mg.%; serum calcium  $9$  mg.%; acid phosphatase  $2.5$  units; alkaline phosphatase  $6$  units; Wassermann reaction negative; Kahn test negative; R.B.C.  $4,610,000$ ; Hb  $87\%$ ; W.B.C.  $5,200$ ; E.S.R.  $12$  mm./hr.; sternal puncture:  $61.9\%$  lymphocytes; other cells normal.

Bone biopsy of skull shows a replacement of the bone-marrow by a fibrous material.

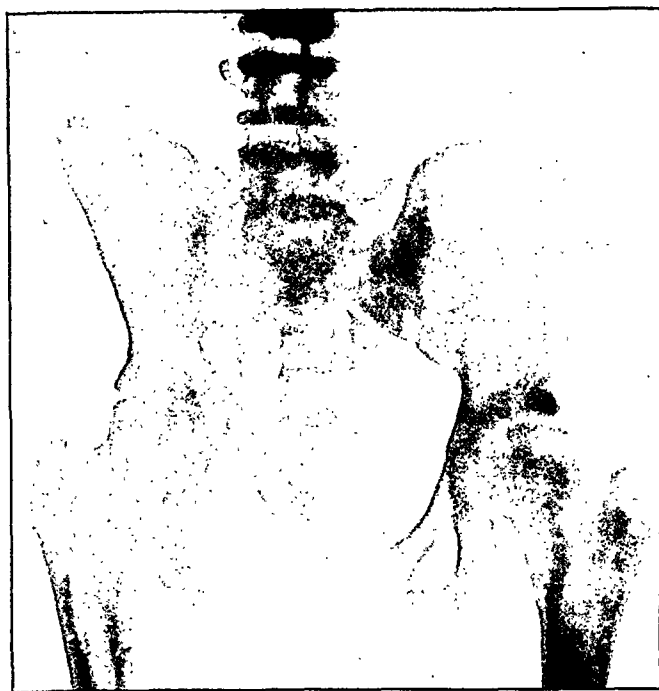
## II. Generalized Osteopetrosis.

A girl, aged 15, complaining of a pain in the sacral area, following a fall. An X-ray revealed a crack in the sacrum and generalized osteopetrosis.

*Family history.*—Only brother, two cousins, and grandfather suffered from osteopetrosis.



(Case II) FIG. 1.



(Case II) FIG. 2.—Showing deformity of pelvis on right side; dense bone in femur, pelvis and lumbar spine.

*Previous history.*—Congenital nystagmus. Left facial weakness which was noted prior to left mastoidectomy, six months ago.

*On examination.*—Palpable thickening of the lower end of both femora. Abdomen: liver and spleen not palpable.

*Blood-count.*—Hb 87%; R.B.C. 4,580,000; W.B.C. 10,200.

X-rays show a dense sclerosis of bone affecting pelvis, spine, skull, lower femora, upper tibiae, and both humeri (figs. 1 and 2). Both lower arms and hands unaffected.



### Bilateral Compound Palmar Ganglia.—ROSS BLOOM, F.R.C.S.

*History.*—Mrs. K. T., aged 28, a housewife, of Boston, Lines, has complained of increasing swelling and deformity of both hands since the age of 12. The swelling started insidiously, first appearing at the base of the left thumb and then spreading to the palm above the wrist and the dorsal surfaces of the wrist. Both wrists were operated on at the Nottingham General Hospital eleven years ago when a "tumour" was removed. The condition was then quite satisfactory for one year but the swelling slowly reappeared. Five years ago, the finger deformity recommenced, spreading from one finger to another. This deformity has been slowly progressive and the weakness of the hands has been gradually more pronounced. She has had slight pain in the hands for the past five years, more marked in the right wrist and occurring mainly in damp weather. She carries on with her duties as a housewife but finds that she cannot wring clothes and also that her hands swell at the end of the day. She has had some swelling of the ankles, left more than right in the past six months.

*Family history.*—No one in her family has a deformity of the hands and wrists.

*On examination.*—A heavy woman, rather obese. Weight  $13\frac{1}{2}$  st. Looks normally healthy. Both hands and wrists show distension of the flexor tendon sheaths. The ulnar bursa is slightly distended. There is a diffuse swelling, in the palms and wrists, of the flexor tendon sheaths. This swelling is of a firm nature and shows no tenderness, heat or redness. There is fluctuation between the palmar and wrist swellings. There is a swelling of the dorsum of both wrists at the base of the thumb and on the radial side of the wrist-joint. There is slight coarse crepitus in the region of the flexor tendons just above the wrist and more marked crepitus in the region of the thumb extensors at the wrist. There is a soft swelling of the flexor sheaths of each finger on the front of the first phalanges where crepitus can be felt, particularly on flexion of the fingers.

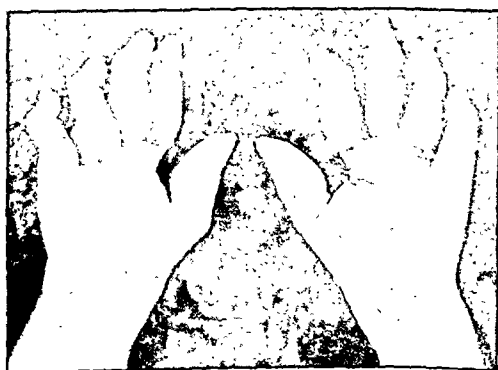


FIG. 1.—Oblique view of hands showing deformity.

*Deformity.*—There is deformity of all the fingers and thumbs on both sides. The thumbs show a flexion deformity at the metacarpophalangeal joints of 20 degrees on the left and 30 degrees on the right. There is a hyperextension deformity of 40 degrees at the interphalangeal joints of the thumbs. The fingers show deformities of 30 degrees hyperextension at the proximal interphalangeal joints, and of 40 degrees flexion at the distal interphalangeal joints (fig. 1).

*Movements.*—Metacarpophalangeal joints of the fingers move normally. The thumb metacarpophalangeal joints flex fully but extension is limited as above. The

first interphalangeal joints of the fingers flex 90 degrees from the position of deformity. The thumb interphalangeal joints flex 80 degrees from the position of deformity. The second interphalangeal joints of the fingers flex 30 degrees from the position of deformity. The right wrist flexes 60 degrees and extends 20 degrees. The left wrist flexes 70 degrees and extends 45 degrees. Forced passive flexion of both wrists is painful (the right more than the left).

*Power.*—The extensors and flexors of fingers and thumb are weak. Abduction and adduction of the fingers are very weak and all the movements of the thumb are very weak. Sensation of the hands and fingers is normal.

There are healed scars on the fronts of both wrists and on the back of the right wrist.

A biopsy of the left wrist was taken in March by Mr. P. H. Newman. He found that the flexor tendon sheaths at the wrist were distended and bulging and on opening the



FIG. 2.—Showing deformity and cystic areas.

thumb jelly-like and yellowish fluid oozed out. Histological report: "Chronic tenosynovitis. Section shows thickening and papillary overgrowth of the synovial membrane, with occasional 'rice bodies'. There is heavy lymphocytic and plasma cell infiltration of the subsynovial tissues but no definite histological evidence of tuberculosis."

The culture was sterile. A guinea-pig, which had been inoculated, died eight days afterwards when no evidence of any infection or of tuberculosis was found.

The ankles show a soft diffuse swelling on the outer sides of the ankle-joints, more on the left than the right. The left knee shows slight crepitus. The elbows show 20 degrees limitation of full extension, 10 degrees limitation of full supination with tenderness and crepitus over both radial heads.

She was apyrexial throughout her two weeks' stay as an in-patient in March 1948.

X-rays of the wrist and hand show extensive swelling of the soft tissues with resulting deformity of the hand. There are some cystic areas in the carpal bones on both sides and there are some changes associated with extrinsic pressure, mainly in the phalanges (fig. 2).

X-rays of the chest, ankles and elbows show no abnormality.

*Blood-count.*—Within normal limits.

E.S.R. 5 mm. in first hour.

*Conclusions.*—A case of severe and bilateral tuberculous tenosynovitis of the wrists with deformity of the fingers. Presumably, this deformity is due to involvement of the flexor digitorum sublimus tendons with overaction of the flexor digitorum profundus tendons.

**Charcot's Disease Affecting Both Knees and One Hip.**—J. S. BATCHELOR, F.R.C.S.

An above-knee amputation was performed on the left side. An artificial limb has been supplied and with the aid of a caliper on the right leg the patient can walk reasonably well.

**Elephantiasis Nervorum.**—P. MARCHAND, M.B. (introduced by K. I. NISSEN, F.R.C.S.).

(A full account of this case with illustrations will be given in the next issue of the *Proceedings*, Section of Orthopædics.)

## Section of Anæsthetics

President—RONALD JARMAN, D.S.C., F.F.A. R.C.S.

[November 5, 1948]

### Recent Impressions of Anæsthesia in the United States of America and in Canada

#### PRESIDENT'S ADDRESS

By RONALD JARMAN, D.S.C., F.F.A. R.C.S.

DURING my recent visit to the United States and Canada, I had the pleasure of going round various hospitals, and making an educational tour of the schools and colleges of New England. I soon realized that no expense had been spared to acquire the best apparatus and equipment available. The shortage of nurses is very acute, leaving the anæsthetist no assistance in the anæsthetic room or theatre unless a student is willing to help. Fortunately the number of postgraduates and nurse technicians is large, as the centres concentrate on making the teaching facilities attractive for them. The postgraduate is eager to get as much experience as possible, so he is willing to assist the anæsthetist when necessary. Teaching for the undergraduate is very limited, he attends lectures for a period of four weeks with very little opportunity of gaining any practical experience. The anæsthetist is entirely responsible for the apparatus in use and for seeing that everything has been sterilized; he also has to assist in getting his own trolleys ready.

Amongst the many large centres in New York City, I visited the Presbyterian, the Belle Vue, the Memorial Cancer, Roosevelt and Cornell hospitals.

Dr. Virginia Apgar is head of the anæsthetic service at the Presbyterian, which is a very fine organization, responsible for running every theatre in the hospital, including the maternity and private operating theatres. She had two fully qualified anæsthetists and six or eight postgraduates in training, and organized them in teams of three which seemed to work successfully, except that the neurosurgeon preferred to work with the same anæsthetist. They were all busy during the day and night work was distributed evenly over the whole group.

Dr. E. A. Rovenstein's service at the Belle Vue Hospital was on a much larger scale as he had undertaken the responsibility of training up to thirty postgraduates, the more advanced students being called upon by other hospitals in the district if their service had broken down.

The two other hospitals were served with anæsthetic chiefs, assisted by students who, in turn, were relieved by nurse technicians. The more difficult cases were taken by the expert, or started by him and then left in the hands of the students and technicians.

The American postgraduate has to spend two years in hospital, not earning very much, then he may go out and practise for three years before being allowed to take his examination, making five years in all. In Canada this is different. The post-

graduate at the McGill University has to take three years, during which time he is studying and doing intern work at the numerous hospitals in the district. A similar plan is established in Toronto. The examination is severe, being written and oral, concentrating on basic sciences and the *vivas* are very thorough indeed. Each student has a practical examination by a visiting anaesthetist.

The standard anaesthetic is similar to ours: suitable premedication, pentothal induction followed by nitrous oxide, oxygen and ether. In a number of cases the pentothal induction is not used. The importance of a good night's rest is recognized, using various drugs, chiefly nembutal, and seconal in varying doses. Premedication is not standardized as it is apt to be here.

Atropine gr. 1/50-gr. 1/100 (1.3-0.6 mg.) combined with morphia gr.  $\frac{1}{8}$ -gr.  $\frac{1}{4}$  (10-16 mg.) is used, or atropine gr. 1/50-gr. 1/100 (1.3-0.6 mg.) with scopolamine gr. 1/200-gr. 1/100 (0.3-0.6 mg.). Omnopon (pantopon) gr.  $\frac{1}{8}$  (20 mg.) and omnopon gr.  $\frac{1}{8}$  (10 mg.) is very rarely used except combined with separate doses of atropine or scopolamine.

Pentothal is generally used for induction and given by the intravenous route or by the rectum.

The strength of the intravenous pentothal varies from 0.5% to 2.5%, never stronger.

The solution for the rectum is 1 gramme per 50 lb. weight (22.6 kg.), the salt being dissolved in distilled water, about 60 c.c.

Avertin is used occasionally but only for head cases though its use is fast disappearing.

Maintenance varies from (a) nitrous oxide, oxygen, with or without ether. (b) Nitrous oxide, oxygen and cyclopropane series. (c) Ethylene oxygen. Vinesthene and trilene.

In all cases absorption technique is used, except where contra-indicated.

For all routine cases a saline and glucose drip was established, with a Y tube so that blood could be given at a moment's notice. Whole blood was preferred to everything else to counteract shock and blood loss, though the gelatin solution and plasma were extremely popular in some centres. The anaesthetist was responsible for all the infusions and their maintenance. In every theatre there were sterile trays and packets containing intravenous, spinal, transfusion and local sets.

The research departments adjoined the operating theatres and their services were available for any problem encountered during the giving of an anaesthetic. The pharmacologist, pathologist, and haematologist, also the research workers in atomic energy were all at the call of the anaesthetist. This, of course, is an ideal situation and helps to solve a large number of problems though it must be pointed out that a great deal of work was being done on the supposed reaction of drugs and gases when the technique of the operator was at fault.

By means of various types of apparatus and subjecting the active radicle of different drugs to radiation, it is possible to trace them throughout the body and thus determine how the various compounds are broken down. This form of research has unlimited possibilities but it is not without its dangers. Research workers who have unfortunately come under the influence of these various atomic rays are a very distressing sight, severe burns and ulcers being the result.

The following are the methods of anaesthesia which are in common use throughout the States and Canada. In intubation, practically all the tubes are passed blind, some with a stilette but, fortunately for the patient, a greater percentage without. A laryngoscope is available if the blind method fails. All tubes are well greased with an oily solution with or without an anaesthetic. To keep the curve of the tubes, they all have wired stillettes which are kept in whilst boiling and removed before using. Macintosh, Magill and other laryngoscopes are in constant demand and Rowbotham's sprays are to be seen in most theatres.

Pentothal and curare are the drugs of choice for intubation, with or without a spray. A very tight-fitting cuff is used for all chest cases. The tubes and attachments are kept in place by adhesive plaster and various head-pieces. The absorption technique is used generally and gives complete satisfaction.

At the Anæsthetic Congress in Montreal it was realized that spinal anæsthesia is on the up-grade in both countries and is used in the majority of maternity cases, the technique being saddle and caudal block. Dr. John Cleland and Dr. Robert A. Hingson gave a most interesting paper on continuous peridural and caudal anæsthesia for obstetrics.

During the lectures we were introduced to the Tuohy needle and the plastic catheter which is boilable and can be thrown away after use. This is a vinethyl catheter and not a polyethylene one which cannot be sterilized. This type of catheter is introduced into the needle and then inserted as far as necessary into the spinal column, left inside and the solution injected when required by means of a syringe. No pathological conditions have been reported though various types of headaches have occurred, but these are relieved by an injection of sodium succinate. The mothers and babies have all done remarkably well, proving this method to be a great success.

Dr. Robert A. Hingson produced an amazing high pressure syringe without a needle. The pressure was over 1,000 lb. per sq. in., which, when released, forced the solution for injection through the pores of the skin without causing pain or reaction. It was felt that this syringe would revolutionize injection methods. Over a million dollars have been spent on its production so far and it is still being improved upon but it is hoped that the syringe will be available some time this year.

Anæsthesia for babies and children attracted a great deal of attention. I was fortunate to see four successful Blalock's operations, two being supervised by a technician and the other two by fully qualified anæsthetists. The anæsthetic was nitrous oxide, oxygen and ether, with a drip saline established by means of a plastic catheter tied into the median basilic or saphenous vein. Where a plastic catheter was not used, a fine needle or glass cannula took its place. The anæsthesia was light in all cases. The immediate recovery of the patient is of vital importance in these enormous hospitals which are so short of nurses, and to ensure a smooth and uninterrupted operating session, recovery wards have been established adjoining the operating theatres. These are fitted up with oxygen therapy, oxygen tents on specially prepared beds, transfusion equipment and the requisite nursing staff. This enables the anæsthetist to be called to any case which may be causing anxiety. Any research work which may have been started in the theatre may be continued satisfactorily in these rooms.

In Chicago all the latest research work on atomic energy affecting anæsthetics is being investigated with incredible thoroughness under the able guidance of Dr. Huberta Livingstone, whose husband is the Tudor Edwards of the States. She demonstrated to me a mechanical vapotester which prevents the possibility of explosions in the operating theatre by recording the strength of ether vapour, also a statometer which records any static changes that happen to be in the theatre. Both these had been used with great success down the coal mines.

Another interesting apparatus which was demonstrated with unqualified success was a magnetic recorder of silent music, which was used for all cases under local anæsthesia as well as dental cases, especially for children or for patients waiting in the anæsthetic room. Stethoscope earpieces were applied to the patient's ears, and the music turned on which was only audible to the patient, though a loud speaker could be attached if the surgeon wished to hear it also. Various records of light music could be played and the patient could make his own choice. Children, undergoing dental extractions, enjoyed this immensely whether they were having a local

or a general. The adults, as long as they were partially medicated, were loud in their praises. The children were supervised by Dr. D. N. Buchanan, late of this country, a very great pædiatrician.

The University of Montreal is an amazing building, all the various departments as well as the different sciences being under one roof. The Dental School gave a first-class demonstration of multiple extractions, all the patients having been premedicated with nembutal gr.  $1\frac{1}{2}$  (0.1 gramme) or a smaller or greater dose, according to the type of patient. This was followed by nitrous oxide and oxygen, with packs and a suction apparatus to hand.

After this, we were entertained by Professor Hans Selye, who demonstrated how he had operated on various rats using 12 mg. of progesterone as the sole anæsthetic. Where half their livers had been removed, it was found that 6 mg. was sufficient to produce anæsthesia, the larger dose becoming lethal. Numerous rats were shown in various stages of anæsthesia, including one which had been operated on. The field for this type of anæsthesia was discussed but it was felt that the experiments were not conclusive enough to be tried on the human being and, in any case, a very large dose would be necessary as was shown in the trial case of a large monkey, which was partially successful.

We returned to Rovenstein's Clinic, where cases of shingles, asthma, hyperpiesis, tuberculous laryngitis, tic douloureux and angina pectoris were all being treated by injections of procaine, using 0.5-2% solution. In all these cases the patients had a course of vitamin-C therapy, combined with glucose D, the reason being that any idiosyncrasy would be obviated. The results for shingles, tuberculous laryngitis and tic douloureux were excellent, but the injection of the stellate ganglion, first second and third ganglia, was not without danger, the pleura being stabbed and an artificial pneumothorax produced. The acute asthmatics got immediate relief and it was felt that this treatment should be extended for other acute conditions.

In cases of painful arthritis, a continuous intravenous solution of 1% or 2% procaine is given for this type of case with varied results. Procaine as a relief against pain was treated with severe reserve in Chicago and other methods would be used if possible. In Toronto, Montreal and New York more and more cases were being treated with a certain degree of success, according to the strength of the solution, though it was considered unwise to use this form of therapy if the course of vitamin C and glucose D was excluded, as procaine is inclined to produce a form of tetany which vitamin C seems to prevent.

I would like to mention the method used to control blood pressure in the Cleveland Clinic. A special suit, which is heat regulated, encases the free parts of the body, such as arms and legs. Various types of these suits were demonstrated and a series of slides shown, demonstrating how it may be controlled.

Various methods of giving blood were then discussed, the use of the arterial route having a large following for immediate and urgent transfusion. The method of draining blood from the patient to an apparatus and returning it, thus controlling the tension in the circulatory system, was described in cases of hypertension or operation on the brain.

## Clinical Section

President —G. E. VILVANDRÉ

[October 8, 1948]

**Subpleural Fibroma with Hypertrophic Osteo-Arthropathy.**—LEO RAU, M.D., M.R.C.P.

October 1946: Mrs. C. G., aged 63. Previously shown at the Clinical Section in December 1946.

*Past history.*—1928: Left breast removed for chronic mastitis. 1934: Operation for fibroid or ovarian cyst. 1944: Operation for varicose veins.

Mrs. C. G. was referred to me for rheumatism of her hands, knees and spine. The general examination in October 1946 revealed marked arthritis: B.P. 160/80 (right) 200/100 (left). There was some narrowing of the right palpable fissure, and enophthalmos. The pupils were equal. There were no further signs.

The radiological examination of the hands and the spine showed hypertrophic arthritis. The radiological examination of the chest showed a large shadow in the right mid-zone. This appeared to be in the fissure between the middle and lower lobe (figs. 1 and 2).



FIG. 1.—24.10.46

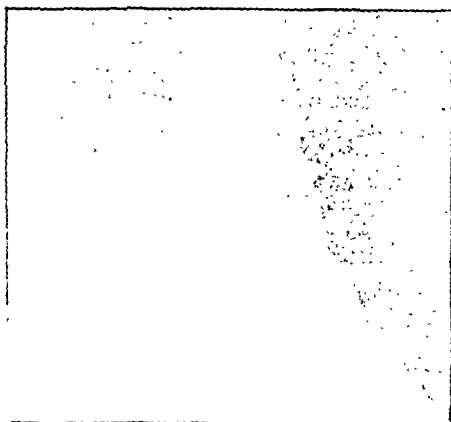


FIG. 2.—11.12.46

*Investigations.*—Blood-count, E.S.R., W.R. in blood, and the Weinberg-Ghedini test were negative. Bronchoscopy (Mr. C. Price Thomas, 6.5.47): Cords normal. Right lateral tracheal wall pushed in. Post-tracheal wall about 1 in. above level of carina had commenced to bulge forwards. This bulge continued into right main bronchus to transverse slit. No actual tumour seen.

*Progress.*—Repeated radiological examination revealed considerable increase in the size of this tumour. Clinically, there was considerable disablement due to the arthritis and Mrs. C. G. had great difficulty in moving about; she had become almost a complete invalid.

*Operation* (Mr. Price Thomas, 8.5.48).—Chest opened through bed of sixth rib. Subpleural tumour found in tissue between upper and lower and middle lobes. Many subpleural vessels were revealed. Pleura was incised and line of cleavage between lung and tumour found. Separation of lung and tumour carried out by blunt dissection. Tumour removed.

*Pathology* (Dr. John Clegg).—Large encapsulated tumour. *Histology.*—Fibroma, with neurogenic elements present.

Patient made a complete, uninterrupted recovery. Within three days of the operation, considerable improvement of the arthritis could be noticed; and within a fortnight no disability was left.

FEB.—CLIN. I



**Comment.**—Joint manifestations may be the initial complaints and the leading symptoms in intrathoracic tumours. They can easily be mistaken for arthritis. The disappearance of these symptoms immediately after the removal of the tumour in a patient who had been almost bedridden and helpless is convincing evidence of the relation of such a tumour to the osteo-arthritis. The original description of this osteo-arthritis by Bamberger and Marie, by whose combined names this disease is often called, was followed by many case reports. The older literature on this subject includes X-ray studies, similar to the one observed in this case, but only recently have there been reports of the successful removal of such tumours resulting in the disappearance of the osteo-arthritis changes. In this case, the pathology was found to be a neurofibroma. Operation revealed no connexion with any anatomical structure.

Severe hypertrophic osteo-arthritis occurs also in carcinoma of the bronchus. In these cases, lack of response to treatment for the arthritis has led to the diagnosis of primary carcinoma of the bronchus.

**POSTSCRIPT.**—When Mrs. C. G. was seen on 15.12.48 she remarked, "I believe it has all come back; look at my hands". The radiological examination revealed the recurrence of the tumour in the right hilar region.

### REFERENCES

- KLASSEN, KARL P., *et al.* (1945) *J. thorac. Surg.*, 14, 407.  
VAN HAZEL, WILLARD (1940) *J. thorac. Surg.*, 9, 495.

**Dr. N. Lloyd Rusby:** The association of gross clubbing of the fingers, and hypertrophic pulmonary osteo-arthritis in other joints, with benign intrathoracic tumours has been recorded, and I have observed an example of a mediastinal tumour, at onset almost certainly benign, in which alteration in the fingers was the main symptom and which had been present for eight years. The nature of the tumour was never disclosed.

Not only does clubbing of the fingers appear to be to some extent reversible and to respond to treatment along with the lung lesion, but in pulmonary suppuration it varies with the clinical condition. In lung abscess, for example, clubbing may become aggravated and the fingers and joints painful when the abscess "blocks"; when drainage is re-established these symptoms abate.

### Rodent Ulcer of Anus.—GERALDINE BARRY, M.S., F.R.C.S.

Mrs. M. A., aged 48. Housewife.

**History.**—Six years ago complained of some irritation round the anus, more so on the left margin. Four years ago a sore red spot appeared to the left of the anus, this gradually increased in size.

Three years ago patient had a hæmorrhoidectomy performed at St. Mark's Hospital. She went back several months later, and she says a portion of the sore was excised for "fester". The sore did not disappear, however, but went on increasing in size. In February 1948 (eight months ago) patient was referred to the Royal Free Hospital V.D. department for treatment of the ulcer on anus. All tests (*see below*) were negative and patient was discharged, condition unchanged. Referred to Surgical Outpatients where biopsy was performed. Admitted to Surgical Ward for excision.



FIG. 1.—Vulva and anus, showing ulcer at anal margin.

**Past history.**—Rickets as a baby. Gonococcal infection acquired from husband in 1930. Bronchitis in 1942. No pleurisy. Syphilis in 1946. Treated with novarsenobillon and penicillin. Three miscarriages. Three children alive and well.

**Family history.**—Mother died of tuberculosis.

**Condition on admission.**—Healthy-looking. Mucous membranes good colour. Weight 8 st. 2 lb. (gain in weight 4 lb. in six months). Appetite good. Bowels open regularly. Micturition normal.

Ulcer on left border of anus, 4 cm. long by 3 cm. in width. The ulcer is shallow, and its floor is raw and red. The base is slightly indurated. The edge is straight and slightly raised above the surrounding area. There is no induration round it. The ulceration extends slightly into the anterior end of the anus, infringing on the mucocutaneous junction. There is slight induration at this spot. Three raised, pearly white patches of epithelialization on the lateral edge of the ulcer are seen. On the opposite side there is indolent ulceration of the right margin, with a raw, rubbed surface and a non-raised edge. This patch is about  $\frac{1}{2}$  cm. in diameter. Ulceration stops at anal

margin (mucocutaneous junction). The right labium minus also shows ulceration on its inner surface. There is leukoplakic change in both labia minora (see fig. 1).

No other abnormal physical signs.

*Investigations* (previous to admission, February 1948).—W. and K. reactions negative. No inclusion bodies or Leishman-Donovan bodies. Frei test negative. X-ray chest: no tuberculosis. Culture: no acid-fast bacilli. Blood normal. No eosinophilia.

*Biopsy of ulcer* (9.9.48).—Epithelial growth arising in the surface epithelium of anal canal, and which in the opinion of the pathologist is a rodent ulcer of pagetoid type (figs. 2 and 3).



FIG. 2.—Biopsy section showing basal cell carcinoma ( $\times 45$ ).

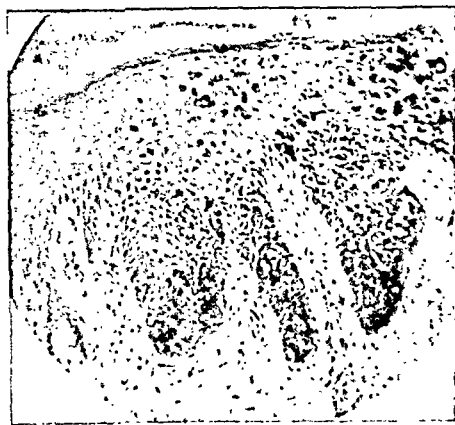


FIG. 3.—Epithelium at edge of ulcer ( $\times 120$ ).

Dr. G. E. Vilvandr  said that in his opinion X-ray treatment was better than surgery for rodent ulcer. Sometimes there was a recurrence after surgery while, for years, excellent results had been obtained by either X-rays or radium in rodent ulcer.

[November 12, 1948.]

**Idiopathic Ulcerative Colitis with Severe Ulceration of the Skin and Peritonitis.**—A. G. LEISHMAN, M.B., M.R.C.P. (for B. BARLING, M.D., F.R.C.P.).

Mrs. L. S., aged 42, was admitted to St. James' Hospital, Balham, in April 1948 with remittent diarrh a for ten years and severe ulceration of the legs.

*History.*—In 1941 she was admitted to hospital with severe relapse of diarrh a, generalized  dema, albuminuria and radiological evidence of an enlarged heart and chronic ulcerative colitis involving the whole colon. The  dema soon subsided, not to recur, but little improvement of the diarrh a resulted from appendicostomy and colonic irrigation.

In 1945 she developed a small indolent ulcer on the dorsum of the left foot which persisted for six months. About that time she had three to six motions daily.

*Family history.*—Mother has rheumatoid arthritis. Patient has one child, and has had considerable domestic troubles.

*Examination.*—A pale, ill-looking but well-nourished woman; temperature  $100.8^{\circ}$  F.; some atrophy of papill  of tongue; koilonychia; lower abdominal tenderness; spleen palpable. Two ulcers were present on the right and one on the left leg, above the ankle, the largest measuring 6 in. by 4 in. and extending round the posterior surface. Walls "punched out" and slightly undermined; the edges thickened and slightly raised; bases greyish, not deep, with  dematous granulations covered with sero-purulent material. Considerable cellulitis and inflammatory  dema to thigh. Six to nine motions daily.

*Blood-count.*—R.B.C. 3,530,000; Hb 48%; C.I. 0.68; W.B.C. 25,300. W.R. and Kahn negative. Agglutination reactions of Salmonella, &c., negative. Sigmoidoscopy showed typical changes of chronic ulcerative colitis in relapse. Barium enema showed involvement of whole colon and about 3 in. of terminal ileum, with much polyposis. Blood culture sterile.

**Liver function tests.**—Total serum proteins: 6.74 grammes; albumin 2.47 grammes; globulin 4.27 grammes per 100 ml. Quantitative van den Bergh 0.2 mg. per 100 ml.; serum alkaline phosphatase 33 units; thymol turbidity test 9 units.

**Course.**—The ulcers on the legs continued to enlarge fairly rapidly, but were controlled with local and systemic chemotherapy. They took six months to heal. During the earlier weeks she developed further tender erythematous swellings on the right leg. Some became fluctuant or bullous and broke down to form phagedenic ulcers with rapid enlargement, the edges dissolving away. Aspiration and penicillin replacement prevented one from ulcerating.

**Bacteriology.**—Cultures from skin lesions in early stages were sterile or Gram-positive cocci of low viability were observed. Swab from colonic ulcer showed *Staph. aureus*, *Strep. faecalis* and *Ps. pyocyanea*.

Her general condition at this time was poor with irregular pyrexia. In May there was a slow onset of abdominal pain with distension and vomiting. Laparotomy four days later showed much bile-stained fluid, intestines matted and covered with flakes of fibrin. No perforation discovered. The wound drained profusely for four weeks.

Thereafter improvement was steady with relief of anaemia; diarrhoea was partly controlled. The liver was palpable.

Total serum proteins: 6.62 grammes per 100 ml.; albumin 2.26; globulin 4.36.

Renal function tests normal.

**Discussion.**—The possibility of hepatic cirrhosis being present was suggested by a palpable liver and abnormal function tests, particularly the failure to restore the albumin/globulin inversion on a high protein diet even though the diarrhoea and anaemia improved. Tumen, Monaghan and Jobb (1947) record cases of cirrhosis associated with ulcerative colitis, including two women aged 14 and 23 years. They believe it to arise as a complication of the colitis and stress the significance of abnormal serum albumin and globulin values and their failure to be restored by treatment.

A period of oedema, albuminuria and cardiac enlargement was considered as being due probably to anaemia and hypoproteinaemia. However, a recent similar case raises the possibility of a vitamin-B deficiency. This was a case with peripheral neuritis which had a fatal issue. Gross cardiac dilatation was found without any demonstrable organic lesion.

Involvement of the terminal ileum is not rare. Crohn, Garloch and Yarnis (1947) record it in about a third of cases of right-sided or segmental colitis which they regard as a small but clinically distinct group, the disease commencing in the proximal colon, the onset being more insidious and the ultimate course severe. This patient conforms to this picture, but evidence of the site of origin of the colitis is lacking.

Peritonitis is uncommon. Usually due to frank perforation, it may result from direct spread through the intact bowel wall. The outlook is said to be more favourable in the latter cases. In this patient it was affected little by chemotherapy.

Skin lesions include erythema nodosum, various septic lesions and rarely severe ulcero-necrotic lesions sometimes called pyoderma gangrenosum. Several American references include Greenbaum (1941), Felsen (1941) and Jones. Butler (1948) recently described 2 cases in this country. The lesions appear to be related to relapse or exacerbation of the colitis with the attendant anaemia and constitutional deterioration; they may affect any part of the body but usually the extremities; they may enlarge rapidly with dissolution of the edges so as, at times, to attain a very large size and endanger life. Healing usually coincides with general improvement of the colitis. Their true nature remains obscure. Butler has summarized the possible aetiological factors and mentions epithelial hypersensitivity for which a case can be made out in this patient.

#### REFERENCES

- BUTLER, E. C. (1948) *Proc. R. Soc. Med.*, **41**, 474.  
 CROHN, B. D., GARLOCH, J. H., and YARNIS, H. (1947) *J. Amer. med. Ass.*, **134**, 334.  
 FELSEN, J. (1941) *N.Y. St. J. Med.*, **41**, 2228.  
 GREENBAUM, S. (1941) *Arch. Derm. Syph.*, **43**, 775.  
 TUMEN, H. S., MONAGHAN, J. F., and JOBB, E. (1947) *Ann. intern. Med.*, **26**, 542.

The report of this meeting will be continued in the next issue of the *Proceedings of the CLINICAL SECTION*.

## Section of the History of Medicine

President—E. ASHWORTH UNDERWOOD, M.A., M.D., D.P.H.

[December 1, 1948]

Sir William Knighton, Bart.  
1776-1836

By HARLEY WILLIAMS, M.D.

### (1) AN ORPHAN OF DEVON

NEVER had the theory of kingship seemed so much at a discount as in the last quarter century before 1800 when William Knighton was beginning his education to become a most successful doctor to a king.

Those American colonists had repudiated King George the Third; the French had put an end to their Sixteenth Louis, and the wearers of every European crown felt uneasy about the head. He was born in the very year when the thirteen Colonies of North America adopted the Declaration of Independence, and he was 7 years old at the close of the American War. When he was 13 he heard of George Washington's election as first President, and how the serious illness of George the Third made it necessary to think of appointing the Prince of Wales as Regent. During such a period of unrest and disparagement of monarchies, this Devonshire boy commenced his most inappropriate training to become a king's physician. His preparation for such a role was entirely accidental. Probably indeed, deep in his soul there did lurk a longing to do great things. But the odds against his climbing to such a lonely eminence as being king's doctor were so enormous that only a romantic boy or his adoring mother could have entertained the notion. William Knighton was to achieve this distinction, but it cannot have been with any premeditation.

William Knighton's father was entirely lacking in talent as a family man. He disappeared, leaving his children to be brought up by their mother. The father of this unsatisfactory parent thereupon endowed his daughter-in-law with five hundred pounds, and the children lived in an atmosphere which was distinctly religious. John Wesley had been preaching in the West Country and had set a high moral tone. The boy grew up with this negative parental example always before him, and then, as though to intensify his deprivation, his mother married a second time, and he had now a stepfather.

Imagine a boy's questions unanswered, his mother's anguish shared, his grandfather's disapproval, and the private theory about that father who must not be talked about. We can be sure the worldly disadvantages of irregular conduct were very constantly before him and the strict outlook of that home formed his character. William grew to be a man of the most honourable standards and strong moral sense, a man who could handle pitch and not be defiled. Yet underneath this virtuous exterior was an unexpressed sympathy with that absent and romanticized parent which broadened to become an instinctive understanding of those primrose paths which were not to be explored except in fancy. Outwardly, William Knighton accepted the pious opinions of those who criticized that erring father, but inwardly, he understood this double standard was not conscious hypocrisy; it was only the continuation of boyish perplexity into adult life.

Whoever could have dreamed that it was just this habit of command and power of sympathy with the profligate, rather than professional attainment, that would make him so successful as a royal doctor?

An uncle happened to be surgeon-apothecary in the market town of Tavistock, and in the days before manufacturing chemists, that meant being an expert botanist and practical gardener. To this uncle, William Knighton was apprenticed. In the daily round, he rolled bandages, compounded draughts, learned to apply leeches to the patients' skin. He followed his master and held the bowl when veins were opened, and, watching the professional attitudes of his teacher, he came to know when people were really ill and how to handle their whims. In the evening he studied Virgil, Homer and Horace, and on Sunday, religious books. For in that century, literature rather than science was the basis of a gentleman's education. It was the wholesome theory of the eighteenth century that a physician ought to be a man of culture.

The American War was over, and the French War had begun. As William Knighton rode along the Devonshire lanes so far without any "Education" in the modern sense at all, he began to feel a need for wider experience. He was 20 years old when he decided to go up to London and study anatomy in the United Hospitals of Guy's and St. Thomas's. Anatomy was as far advanced in the eighteenth century as it is today, and there were brilliant virtuosi who could teach him. At 21, he was appointed Surgeon to the Royal Naval Hospital at Devonport, near Plymouth, and married the daughter of a Captain of one of His Majesty's ships.

Knighton was always a hard worker and he kept up his reading early in the morning, while the evenings were spent at balls and parties, among the Admirals and Commanders who were home from the French Wars. Knighton was no innovator, he saw within himself no possibility of making scientific discovery, and believed that the key to the mysteries of medicine was to be found in books. Yet the more he read, the further did those mysteries recede, and he was obliged to conclude that, "Medicine was one of those ill-fated arts whose improvement bears no relation to its antiquity". Such was not the temperament likely to make him another William Harvey, and that of a great leader of medicine was the least likely role he conceived himself as fitted to play. But there was one aspect of medical practice for which he developed a decided flair.

The naval captains and their wives, merchant adventurers of old Plymouth, these formed the raw material on which he learned that peculiar craft which he was to use with such an infallible touch as royal doctor. They came to him not only with the honourable wounds of war, but with their livers deranged by Peninsular port and tropical fevers; they turned to Dr. Knighton when pursued by scandals and tortured by the maladies of indiscriminate love, and his keen eyes learned to read their faces. Though he might make no vital discoveries in medicine, he was learning to handle wayward human nature. It was strange that such a man should possess this insight, for he seemed to have no failings. He was only in the twenties, but he looked and behaved like a man of 40, and he was the sort of physician of whom his patients are rather scared.

William Knighton began to be impatient and ambitious. He needed some sort of handle to his name and he managed to put together some first-hand observations and second-hand quotations in the form of a thesis which he despatched to the College professors in the University of Aberdeen at the opposite end of Great Britain, and they granted him a diploma. Now he can carry his cane with greater confidence among his fellow practitioners of the West Country.

He might have settled down permanently to that satisfying existence, but personal tragedy intervened. Knighton passed through a personal trial which increased his disgust for the meagre resources of medicine. His little boy died of one of those obscure and irremediable illnesses that seem especially liable to occur in doctors' families, and impulsively William Knighton threw in his hand. The Devonshire man sold his practice and decided to make a start in London.

Professionally speaking, the London of the 1790's was not so easy for an outsider as Plymouth had been for a native of Devonshire. The fashionable practice was a monopoly of the Fellows of the College of Physicians and Knighton applied for membership of the College, but was not allowed to sit for the examination because of some rule about previous residence which had not been put into operation.

He was admonished by the Royal College of Physicians for practising without a degree, and a second time he gave up the struggle. This time, he went to Edinburgh, then called "the Athens of the North", where a complete course of medicine was given in the Old College. And to make certain of his professional standing, he petitioned the Archbishop of

Canterbury to confer upon him a Doctorate. At last he managed to become a member of the Royal College of Physicians and, now better equipped to conquer the capital, he started practice in the year 1806, determined upon wealth.

William Knighton was upright and clear principled, but he never pretended to be indifferent to money. "It has been said", he wrote, "that riches keep out only one evil, namely poverty, but it has been well said, by a sensible woman, what good can they not let in?" A man possessing natural insight into human nature, coupled with such worldly wisdom was sure to succeed, and he began to find practice in London more to his taste than in a small provincial town. In the Metropolis, one circle led to another, the second often more valuable than the first. A London doctor was less exposed to "the tricks of the trader and the fire of the Brandy merchant".

Now fate, in the disguise of war, carried Knighton on with swift steps. War, says Thucydides, offers a man a destiny which he cannot refuse. The protracted struggle against Napoleon had dragged on for years without interfering very much with the ordinary life of a medical practitioner in the West End of London, but now, when he was 30, William Knighton was swept into new existence. Lord Arthur Wellesley was going to Spain upon a special embassy, and he invited Dr. Knighton to go with him as personal physician.

Following his Lordship through that dusty and tragic land, staying at palaces, monasteries and inns, the doctor had every opportunity of watching how great affairs were conducted. He noted, he absorbed and he was very discreet.

During the four months of the Mission, he wrote home to his wife the most affectionate and graphic letters, describing the kindness of Lord Arthur, the terrible oppression of the heat, that wonderful canvas of Murillo he had seen in Seville Cathedral. In Spain he saw grandeur and misery at close quarters, and became confident of his power to work the physician's spell.

When the Mission was over, his patron recommended him to George, Prince of Wales, who was one of these natures who have, for one reason or another, perpetual need of doctors. Dr. Knighton was duly presented at Carlton House. His professional preparation was over. At last his remarkable career was to open.

## (2) THE PRINCE'S PHYSICIAN

He entered the bedroom, knelt and kissed the Prince's hand. There before him was the face upon which he was to learn to play as on an instrument, a face of a thick dusky hue, almost copper colour, with the most fascinating expression hinting at a mind intelligent though easily moved to suspicion. The Prince was suffering from lameness, perhaps from an accident, or his abuse of laudanum, and several of his doctors stood in attendance, for the Prince liked to be surrounded by medical men, whom he used for all kinds of whims, it being his royal pleasure to treat his doctors like upper servants. On this first occasion, Knighton was not invited to prescribe, a circumstance which was indeed fortunate for him, since he was quite at sea as to the meaning of the Prince's complaints. So the doctors in regular attendance were denied the gratification of seeing this newcomer and potential rival make a fool of himself. But they were not pleased when, after Knighton's departure, the Prince remarked that he was the best-mannered medical man he had ever met. It was the royal humour to tease his physicians.

Next time Knighton went to Court, he felt something wrong, and suspected rightly the malevolent influence of his professional brethren. The Prince frowned and showed displeasure. Knighton was mystified, until he learned that lying tongues had reported him as having criticized the Prince's conduct towards the Princess of Wales. After a few days, however, this misunderstanding was removed.

Among the most favoured of these medical attendants was a noisy Irishman named Sir John MacMahon. In his heyday he had been a close confidant of the Prince, but now he was rapidly going to seed, and he was apt to be indiscreet in his cups. It was becoming obvious to the Court that old MacMahon had reached the end of his professional usefulness. But who was to inform the Prince? The royal doctors took counsel and decided that the best person to carry out this disagreeable job was their new colleague. In arranging this they did not intend any favour to the upstart. Yet the awkward embassy was to prove Knighton's final entrance into the Prince's intimate favour.

As he listened to Knighton's report about the state of Sir John MacMahon's health, the Prince Regent became disturbed. He was worried on the subject of certain private papers which the old physician possessed, and at the close of the interview, he made his wishes perfectly clear. Knighton was commanded to persuade MacMahon in three directions: first to resign, secondly to propose Sir Reginald Blomfield as his successor and, most important of all, to yield up those personal letters.

This Blomfield, though nominally one of the private physicians, kept his place at Court mainly through his good looks. He was now, on the retirement of Sir John MacMahon, to succeed him as keeper of the Privy Purse, and it seemed that Knighton had been the instrument of placing someone ahead of himself in that race for privilege, though he had done it at the Regent's personal desire. He was to find that willingness to bow to such whims was the surest means of advancing his personal status.

Gradually, Knighton moved ahead of his rivals in the service of this fascinating egoist who was ruler of England. He had managed to extract from the dying MacMahon those papers about which the Prince Regent was so anxious, and now His Royal Highness was obliged to divulge that the letters came from a certain Mrs. Fitzherbert who had been a bosom friend of the late Sir John. Of course, this Mrs. Fitzherbert was none other than the notorious lady who claimed to be the Prince's legal wife, and he now unburdened his soul to his new physician.

They had both been young, so the Prince explained, Mrs. Fitzherbert 30 and himself only 23, and a clergyman had been sent for to read over a few lines just to please the lady, but there had been no proper marriage licence. They had taken too much wine and the whole thing had been in fun, just a piece of play-acting. From the Prince's own lips, Knighton heard this sordid tale which he knew at least in outline, from the gossip of every drawing-room. This squalid performance had become much more than a broken romance. The lady happened to be a Roman Catholic, and she and her friends professed to regard this irregular episode in Park Street as the celebration of a Sacrament, and declared that if everyone had her rights, Mrs. Fitzherbert was the wife of the Prince Regent, and heiress to the throne of England.

The new physician listened. Something drew him powerfully towards this troubled royalty with the large eyes, sensual lips and mixture of dignity and commonness, but he concealed his thoughts.

His loyalty gave the Regent confidence, and he was now entrusted with a further and even more delicate commission, for the consequences of Mrs. Fitzherbert were by no means over. The lady possessed still more letters written by the Prince, and these Knighton was commanded to secure in exchange for those of hers which had come to light from the papers of Sir John MacMahon. Knighton went down to her house at Brighton and when she refused to see him, saying she was ill, he insisted on the privilege of a doctor, walked into her bedroom and bullied her. But Mrs. Fitzherbert was too artful. She produced some of the Prince's letters but kept back others, and later she even trumped up a story that Knighton had not handed over to the Prince all the letters which MacMahon had given him.

But the mission to the lady's bedroom at Brighton had been not entirely unsatisfactory, the Prince Regent thanked Knighton warmly, and he rose like a meteor over the heads of his brother physicians.

Wherever he was, at Carlton House, or Brighton, the Prince must always have him near at hand, and when he came to the throne as George the Fourth, Knighton was taken on a tour of the German dominions, and the man who had worked so hard to get his medical diploma at Aberdeen, and who had petitioned the Archbishop of Canterbury for a parchment, was now invested with an *honorary* Doctorate of Medicine of the ancient University of Göttingen, being presented therefor by the Duke of Cambridge. He was given the Grand Cross of the Teutonic Order of Guelph, and appointed to a lucrative office in the Royal Duchy of Cornwall. In 1812, he became a baronet, and when that other Royal Physician, Sir Reginald Blomfield, became a peer and Minister to Sweden, Knighton succeeded him as Keeper of the Privy Purse and King's Private Secretary. In 1822, he wrote his last medical prescription and became entirely the King's man of business. There was even an attempt to make him Chancellor of the Duchy of Lancaster, but for once political influence was too strong.

But he was sufficiently secure in the King's friendship. It was enough that he could receive letters signed G.R. and beginning "Dearest Friend", and expressing sentiments such as these: "It is utterly impossible for me to tell you how uncomfortable and how miserable I always feel when I have you not immediately at my elbow."

### (3) MASTER OF THE HOUSEHOLD

Sir William's psychological link with the royal libertine was an attraction of opposites. George the Fourth trusted him, feared him, and in time would come to hate him. Knighton now handled all the King's correspondence. He was directed to undertake "the entire management of our private affairs with a view to the observance on the most strict and rigid economy, that we may have the opportunity of relieving ourselves from certain em-

barrassments which it is not necessary to mention further in detail". Sir William even began to have influence in making and unmaking the King's Ministers and, naturally, this did not please the elder statesmen. His former patron, Lord Arthur Wellesley, now Duke of Wellington, wrote advising him not to meddle in affairs which did not concern him, but the Keeper of the Privy Purse gave a demonstration of his new power by taking this letter straight to the King, who thereupon haughtily observed to the Duke, that Sir William was responsible to himself alone.

But the most onerous responsibility of the King's private secretary was the delicate duty of managing the royal ladies, and here Sir William Knighton showed superlative talent.

Lady Conyngham had appeared on the scene as royal favourite, and fortunately, Sir William found her more easy to handle than Mrs. Fitzherbert had been. Lady Conyngham had a husband of her own, but she was treated as the suzeraine of Carlton House. Experienced judges of court magnificence had never seen anything so fine as the pearls she wore, and one evening Sir William Knighton particularly noticed, sparkling in her head-dress, a very large sapphire belonging to the Crown Jewels of England which had come down from the Stuarts, and next day he let it be known that he had observed her Ladyship wearing that particular sapphire.

Lady Conyngham became entirely subservient to him, so afraid was she of his influence with the King, and would not invite to dinner anyone of whom Sir William disapproved. And he kept his eye upon her and saw to it that those wonderful sapphires came back to their rightful place among the Crown Jewels of England.

Knighton was now one of the most powerful men in England, and anyone who wanted a royal favour wrote to him. Lord Liverpool thanks him for the King's gift of a thousand pounds to Trinity College, Cambridge. Sir Walter Scott writes to ask if he may use in a forthcoming book a letter from Lord Byron quoting an opinion from the Prince Regent, and adding, perhaps not entirely as an afterthought, that the *Waverley Novels* are selling well and he hopes copies have been placed regularly on His Majesty's table. George Canning writes to him for permission to take his wife to walk under the trees of the Pavilion gardens at Brighton. It was Knighton who commissioned from Sir Thomas Lawrence the fine series of portraits which formed the King's collection.

Mrs. Fitzherbert had not been the only royal indiscretion, and now the tangled errors of the past had become an obsession with the King. Who could sort them out but his ever-resourceful friend? Sir William Knighton was to have many opportunities to prove his diplomacy, and an important part of his duties came to be to range all over Western Europe, setting out often at short notice, as each fresh embarrassment came to the King's attention. To Paris, Spain, Belgium and even Sardinia, he travelled to collect and suppress. Wherever he went he visited picture galleries and churches and museums, he listened to music, and in his diary he wrote an account of his personal relaxations, but never of his official duties. He eliminated the evidence with the firmness of a faithful servant. His determination to keep the King's secrets was so successful that all the knowledge we possess now is nothing but a mere fragment of that immense web of intrigue.

The tone of the King's letters to his Keeper of the Privy Purse is sometimes that of a suppliant. The royal quill would cover sheets of paper with commands that read more like entreaties, as though he were in the power of Sir William Knighton.

And the man who had been the royal doctor never failed.

#### (4) MENTAL ASCENDANCY

For such immense but unmentionable services, the First Gentleman in Europe would shower his Private Secretary and Physician with gratitude. Then, as his mood changed, and Sir William was no longer in the presence, the King might repent of his repentance and write a long tortuous letter undoing what had been said, but with quaint consideration ordering the messenger not to deliver it before five in the morning in order not to disturb Sir William's repose. "I am ready", wrote the King in one of these moments of stiffening dignity, "and prepared to act upon and to meet with even the very essence of all that conciliation, all that good temper, all that the strictest sense of honour and liberality can dictate." Then, as though he feared the result of such magnanimity, his sentiments rose in a crescendo of self-justification and much underlining with the quill. "But let the stake be what it may, and the risk however great, I must not, I can not, and more I will not tolerate even the possibility of the most trivial breath of inconsistency as of duplicity being affix'd upon me or my character. I know I may repose myself in perfect confidence in your hands and that (however difficult the chrysis may be) you will exert yourself in this cause, upon the same principles of conscientious rectitude which alone actuate me."



What, we may ask, was this royal victim of paranoia afraid of? To us, the career of George the Fourth seems so loaded with scandals that one or two more might have been unnoticed. But the King's sense of his personal honour was morbidly acute. The sordid revelations of his divorce, that shocking moment in his life when the Princess of Wales knocked on the door of Westminster Abbey demanding to be crowned as his consort, these and countless other misadventures troubled the King's imagination, and made him dread the ridicule of the world. In the crowd of courtiers and sycophants there was only one whom he could trust. Now and then this man was obliged to disobey the King's command. "I am so surrounded with cares on your Majesty's account", wrote Knighton, "So separated from every kind of support but what I derive from my own intellectual efforts that when I say happiness and myself are strangers, I do not mention it in the language of complaint, but only to hope that when I venture to oppose any of your Majesty's commands, your Majesty will believe it always arises from these feelings of devotion and honesty which are the true characteristics of my nature towards your Majesty."

The King knew his man, knew his loyalty, and felt for him genuine affection. "Let me implore you to come to me, be it but for a moment, the very first thing you do this morning; for I shall hate myself until I have the opportunity of expressing personally the pure and genuine feelings of affection which will never cease to live in my heart so long as that heart continues to beat. I am too unhappy to say more, but that I am ever your affectionate friend, 'G.R.'."

Such was the nature of this reciprocal feeling between the Physician and the Monarch. But no human being, least of all George the Fourth, could endure easily the thought of being in another man's power, and underneath his protestations the King both feared and hated his doctor. On one occasion when the sovereign was making merry with some Tyrolese dancers and thoroughly enjoying himself, he called out that he would give ten guineas to be able to see Knighton's face if he should walk into the room and see them at play like servants merrymaking in the master's absence.

Another time, with his attendants all around him, George the Fourth cried out that he wished to God some one would assassinate Knighton. One of his royal predecessors six hundred years before had made a similar ejaculation which caused a murder in Canterbury Cathedral. This time the King was preserved from the ill-fortune of being taken seriously. But Knighton made him tremble. That efficient and discreet servant who knew his weaknesses so well could cause his master's handsome and self-indulgent face to darken and the flabby cheeks to melt. The royal exhibitionist, who never concealed his faults from his valets, had a deeper level of frailty below what he would admit even to himself, and even this unfathomable depth was known to Sir William Knighton. Deeply he despised the man even while he gave profound respect to the King, and he took no trouble to hide what he thought. There is one famous remark of his which expresses a whole volume. George the Fourth when in his cups was given to a riotous range of fancy, and on one occasion he was describing to his astonished but discreetly silent courtiers the Battle of Waterloo and the orders in the field which had been given on that famous occasion. The whole success of that occasion, it seemed, had been due to the King's personal strategy.

We can picture Sir William Knighton's severe smile when this royal extravaganza was reported to him, and he remarked: "Let his Majesty but give up Curaçoa, and he will win no more victories."

A man who had obtained so unusual an ascendancy paid for his eminence much more than he ever received in gratitude. Under the pretence of solicitude for the King's interest, people attacked the Keeper of the King's Private Purse. A maiden speaker in the House of Commons launched a ferocious attack upon him; but it exploded like a damp squib and left Knighton undisturbed in the royal favour. One horrified official who came away from the royal presence told observers that he had actually heard Knighton contradict the King without ceremony or circumlocution, and that Knighton had even gone the length of cross-questioning, whereat George the Fourth, giving Knighton permission to finish what he had already begun, said, "You may ask him what questions you please: he is the poorer man for having known me," and held out his hand to be kissed. In this mood he would pour out self-justifying letters to his confidant. "You know how honourably and fairly I have conducted myself to all parties; notwithstanding all the warmth of friendly advice I have given, everything that passes under the eye of the public proves but too much and too sensibly that is entirely disregarded and complete without weight and therefore entirely cast aside—"

The troubled King, now well on in his sixties, suffered greatly from bladder irritation, probably due to a stone; he constantly took laudanum, and hardly ever went out of his overheated rooms where he passed the days morosely comparing his symptoms with those

of which his brother the Duke of York had died. His Majesty had even abandoned the attempt to preserve his figure, and allowed his belly to descend to his knees. Fear of death, fear of illness, fear of Sir William Knighton, these haunted George the Fourth in his last years. Yet he clung to his adviser. "Though blind as a beetle, I endeavour to scribble a few lines," he wrote mysteriously on a very familiar theme, "All at present is buried in my own breast and communicated to you alone. --- My main object is to arrange everything with you and to ensure quiet and comfort, before any alarm can be given rise to however absurd, from any cause, but most especially before either any vague report or article copied from foreign papers may reach us here." This, written in the King's last year of life, shows that his morbid fear of public ridicule was still warm.

Owing to cataract in his eyes he could hardly read, and at Privy Council meetings candles had to be held at a particular angle to enable him to get through his speech. He feared the fate of his father, George the Third, who had become both blind and mad. The acid-tongued Greville said that George the Fourth was already a little of both. But in spite of everything, Knighton's devotion never wavered. As the King entered upon the final phase of his earthly existence, the Privy Purse saw the decline and wrote to his wife from the royal bed-chamber: "We are not going on well: depend on it, this will not do: if this illness should be protracted, I see much suffering and embarrassment before us --- my duty is to promote the King's comfort and peace of mind: I will never consent that he shall have a moment's pain, to gratify the idle curiosity of a set of persons whose only objects are - to find fault with everything and to pull down, if they possibly could, the character of the individuals who are endeavouring to serve their sovereign by every means in their power." He placed, unasked, a large-type bible on the King's dressing table, with which His Majesty was much pleased.

#### (5) THE WATCH-DOG AT WINDSOR

As the King sank more deeply into the illness from which he never recovered, no one realised better than the Keeper of the Privy Purse that the termination of his own professional career was approaching too. He kept an even more vigilant eye upon the Crown Jewels which Lady Conyngham would have liked to appropriate, though by now she had long been bored with the King. Nevertheless, wagon-loads of royal possessions were passing from Windsor to her house, and a few days before the King's death, Sir William performed his last service to his master. A mysterious financial transaction was passed through quite without a trace or record.

Thirty thousand pounds' worth of stock belonging to the King was sold; the proceeds disappeared into thin air, but everyone believed the money had gone to Lady Conyngham. This inflexible Keeper of the Privy Purse, who despised mistresses as much as he despised the man who kept them, made his last gesture of absolute power, as he handed over money to the woman who had been so timid of losing his favour. Thereby he brought to an end worldly authority over her and others whom he had disciplined for the King's good. It is a tribute to Knighton's character that no one suspected him of appropriating this money for himself. And here, at the risk of being too psychological, we must remind ourselves of Knighton's boyish dilemma between that secret sympathy with his erring father and the strict moral standards of his fatherless home. The King knew, everyone knew, that Sir William Knighton was endlessly indulgent to his master's whims, yet fundamentally incorruptible.

The royal illness worsened, but still Knighton thought it might go on a few days further. Then came the summons, and he was called from his rooms in the Lancaster Tower to the private apartments, just in time to witness the last sigh. "Thus ended," he wrote, "the life of George the Fourth, one of the most accomplished men in Europe—full of benevolence. There will be many to deplore his loss."

After the King's death, the Duke of Wellington opened the private *escritoire* and could not find enough to pay the messengers who were despatched all over the kingdom with the news, and while the valets were unearthing a prodigious quantity of trinkets and trash, women's hair of all colours and lengths, some with powder and pomatum sticking to them, notes and letters and feminine gloves, Sir William stood by and saw that nothing of value disappeared. Suits worn for fifty years, every sort of uniform, three hundred whips, and dozens of riding breeches, furs, pelisses and hunting coats—enough to stock Drury Lane Theatre, these trifles were sold by auction, while the royal watch-dog stood guard over the apartments, alertly keeping his eye both upon Lady Conyngham, and the key of the King's jewel box. Thanks to his fifteen years of vigilance the King died out of debt.

#### (6) A PHYSICIAN'S REWARD

Sir William Knighton was a physician in the age of personal influence, when almost the doctor's sole resources was an intuitive understanding of the patient's temperament. He

ceased to practise medicine, but he never ceased to use this extraordinary personal gift. George the Fourth changed his Prime Ministers often, but he trusted absolutely to Knighton's integrity, though dreading the silent reproaches of his eyes; chafing over his dependence upon the guardian of his disreputable secrets, yet quite unable to do without him. They understood one another perfectly, but Knighton had the fewer illusions. Bullying discarded mistresses—not a very becoming occupation for a doctor! But neither was the indiscriminate pursuit of them very ennobling in a king. We should not apply modern morals to this case. We can only marvel that an honourable man could stoop occasionally to such sordid transactions without becoming corrupted by them.

Among memorable physicians, Sir William Knighton finds a place not for his knowledge of pure medicine or for any skill in treatment. He was great only as a guardian of His Royal Patient's soul. He performed that fundamental service which every doctor must first give to his patient, that of providing mental assurance. Knighton did this superbly, because he understood the human organism in all its weakness. Yet, at the same time, he himself was supremely robust. In the portrait of him by Sir Thomas Lawrence, in a neck-cloth and unbuttoned surtout, looking as though he had just dismounted from horse, we see a firm-willed, cheerful man, who looked life in the face and saw more good there than evil. In the letters he wrote to his children, we see that the orphan boy of Devon has become a good father, humorous, understanding, indulgent, though inclined a little to religious moralizing that nevertheless sounds transparently sincere. The last letter he ever wrote to his son who had become a painter speaks of a colourful gipsy girl who was to sit as a model.

Knighton's vivid diary is silent upon the subject-matter of his secret missions. It was something more than discretion. At heart he was a man of intense sympathy, but there were certain experiences which his inhibitions simply would not allow him to write down. That alert royal servant who rattled in his coach over the Continental highways to interview discarded mistresses was the puritan in whose soul there lurked a libertine. The Devonian boy had felt the appeal of John Wesley telling him that the good life was more than a King's crown; yet blood was strong, and George the Fourth attracted him like a psychological magnet through a remembrance of his own father, and a boy's sympathy, overlaid by a lifetime of rectitude, made him indulgent. This clear-sighted man never forgot that Prince Charming with the curled hair and fine eyes who had fascinated him on the first audience. Each time he returned to Carlton House with a new bunch of letters and a strict account of the guineas spent in obtaining them he received from that corpulent gentleman who sat sideways upon the throne of England the accolade of gratitude. No statesman, no mere private secretary, would ever have been given that sort of appreciation. The King's friend could have had any reward for which he cared to ask; but he never enriched himself. He was content to remain the most powerful private person in England, and when George the Fourth died, he quitted the spheres of power and devoted himself to the enjoyment of painting and the solace of travelling through Europe.

He had been permitted to see the very worst in the King's heart only because he was trusted absolutely. Often he saw the dignified character emerge from behind the self-indulgent mask, and in those moments tasted that exquisite sensation of authority which triumphant virtue has over humbled vice.

*The above paper is much abbreviated from a chapter entitled "Three Royal Physicians". This is taken from a book called "The Healing Touch" which is to be published by Messrs. Jonathan Cape during 1949.*

# PROCEEDINGS *of the* ROYAL SOCIETY OF MEDICINE

ISSUED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE:

HONORARY EDITORS

ERIC A. CROOK      E. R. CULLINAN

EDITOR

J. M. BROWNE KUTSCHBACH

|                                           |                                 |
|-------------------------------------------|---------------------------------|
| G. S. W. ORGANE (Anæsthetics)             | F. T. RIDLEY (Ophthalmology)    |
| J. S. RICHARDSON (Clinical)               | H. L.-C. WOOD (Orthopædics)     |
| J. B. BROOKSBY (Comparative Medicine)     | C. S. HALLPIKE (Otiology)       |
| E. W. PROSSER THOMAS (Dermatology)        | A. G. SIGNY (Pædiatrics)        |
| E. F. SCOWEN (Endocrinology)              | F. R. SELBIE (Pathology)        |
| ALLAN McFARLAN (Epidem. & State Med.)     | M. B. RAY (Physical Medicine)   |
| A. C. WHITE (Exper. Med. & Therap.)       | O. V. LLOYD-DAVIES (Proctology) |
| I. E. McCracken (History of Medicine)     | DENIS HILL (Psychiatry)         |
| W. A. MILL (Laryngology)                  | F. CAMPBELL GOLDING (Radiology) |
| MAURICE DAVIDSON (Medicine)               | CHARLES DONALD (Surgery)        |
| J. St. C. ELKINGTON (Neurology)           | G. M. FINDLAY (United Services) |
| LESLIE WILLIAMS (Obstetrics & Gynæcology) | A. CLIFFORD MORSON (Urology)    |
| B. W. FICKLING (Odontology)               |                                 |

SECRETARY OF THE ROYAL SOCIETY OF MEDICINE  
G. R. EDWARDS



NEW PRESENTATION  
25 mg. Glossettes.

REDUCTION IN PRICE  
of 5 mg. Glossettes.

# METHYLTESTOSTERONE

TAB. METHYLTESTOSTERON  
GLOSSO-STERANDRYL—25 **25 mg. (ROUSSEL)**

SUBLINGUAL ADMINISTRATION

**NOW IN TWO STRENGTHS**

**5 mg. and 25 mg.**

## ADVANTAGES OF THE 25 mg. GLOSSETTES

**Small Doses:** One 25 mg. Glossette per day, instead of five 5 mg., obviates the inconvenience of having to retain them in the mouth for a period five times as long.

**High Doses:** Until now, there has been no convenient method for the sublingual administration of high doses of male hormone. This is now possible using repeated daily administration of the 25 mg. Glossettes.

**IN THE MALE:** Hypogenitalism, Male climacteric, Senility.

**IN THE FEMALE:** Metrorrhagia, Premenopausal disorders.

5 mg. Glossettes: 20...12/9, 100...57/6, 500...266/-  
25 mg. Glossettes: 10...28/-, 20...56/-, 100...252/- 250...610/-



**ROUSSEL LABORATORIES LIMITED**  
95 Great Portland Street, London, W.1. LAN 3744

# PROCEEDINGS

## OF THE

# ROYAL SOCIETY OF MEDICINE

Vol. XLII    No. 4    April 1949

## CONTENTS

Whole  
Proceedings  
Page

### Section of Comparative Medicine

|                                                      |     |
|------------------------------------------------------|-----|
| DISCUSSION: LIVER DAMAGE OF METABOLIC ORIGIN .. .. . | 201 |
|------------------------------------------------------|-----|

### Section of Epidemiology and State Medicine

*November 1, 1948*

|                                                   |     |
|---------------------------------------------------|-----|
| DISCUSSION ON THE PREVENTION OF ACCIDENTS .. .. . | 207 |
|---------------------------------------------------|-----|

*December 6, 1948*

|                                      |     |
|--------------------------------------|-----|
| DISCUSSION ON FOOD POISONING .. .. . | 214 |
|--------------------------------------|-----|

### Section of Surgery

|                                              |     |
|----------------------------------------------|-----|
| DISCUSSION ON HIRSCHSPRUNG'S DISEASE .. .. . | 221 |
|----------------------------------------------|-----|

### Section of Experimental Medicine and Therapeutics

|                                                                                                                                     |     |
|-------------------------------------------------------------------------------------------------------------------------------------|-----|
| The Place of the Experimental Method in Medicine —President's Address by Professor<br>G. W. PICKERING, M.A., M.B., F.R.C.P. .. .. . | 229 |
|-------------------------------------------------------------------------------------------------------------------------------------|-----|

### Section of Medicine

*November 23, 1948*

|                                                                   |     |
|-------------------------------------------------------------------|-----|
| DISCUSSION ON CHRONIC DIARRHŒA, EXCLUDING TROPICAL CAUSES .. .. . | 235 |
|-------------------------------------------------------------------|-----|

*January 25, 1949*

|                                                                                                          |     |
|----------------------------------------------------------------------------------------------------------|-----|
| DISCUSSION ON THE PLACE OF ARTIFICIAL PNEUMOTHORAX IN THE TREATMENT OF PULMONARY<br>TUBERCULOSIS .. .. . | 244 |
|----------------------------------------------------------------------------------------------------------|-----|

### Section of Odontology

|                                                                                                                                     |     |
|-------------------------------------------------------------------------------------------------------------------------------------|-----|
| Dental Caries in Norwegian Children During and After the Last World War. A<br>Preliminary Report.—By GUTTORM TOVERUD, Ph.D. .. .. . | 249 |
|-------------------------------------------------------------------------------------------------------------------------------------|-----|

(Continued on next page)

## Section of Endocrinology

|                                                                                                                  |     |
|------------------------------------------------------------------------------------------------------------------|-----|
| Addison's Disease.—R. I. S. BAYLISS, M.R.C.P., and RUSSELL FRASER, F.R.C.P.                                      | 259 |
| Addison's Disease Treated by Adrenal Grafting.—Shown by A. ELTON, F.R.C.S., for L. R. BROSTER, O.B.E., M.Ch.     | 260 |
| Simmonds' Disease following Haematemesis. Gastric Ulcer.—Q. HOBSON, B.M., M.R.C.P., and RUSSELL FRASER, F.R.C.P. | 262 |
| Post-traumatic Pan-hypopituitarism.—A STUART MASON, M.B., M.R.C.P.                                               | 263 |
| Thyrotoxicosis, Exophthalmic Ophthalmoplegia, Myasthenia Gravis and Vitiligo.—RAYMOND GREENE, D.M.               | 263 |
| The Use of Adrenocorticotrophin in Testing for Adrenal Insufficiency.—F. T. G. PRUNTY, M.A., M.D., M.R.C.P.      | 267 |

## Section of Orthopaedics

|                                                                                                             |     |
|-------------------------------------------------------------------------------------------------------------|-----|
| Engelmann's Disease.—L. S. MICHAELIS, M.D.                                                                  | 271 |
| Pathological Fracture Through a Cyst of Scapula.—J. F. PAXTON, F.R.C.S.Ed. (for St. J. D. BUXTON, F.R.C.S.) | 273 |
| Fractured Lunate Bone Replaced by Plastic Cast.—E. L. TRICKEY, M.B., B.S. (for St. J. D. BUXTON, F.R.C.S.)  | 274 |
| Rupture of Tuberculous Paravertebral Abscess into Pleural Cavity.—M. ALBERT, F.R.C.S.                       | 275 |
| Osteogenesis Imperfecta in Father and Son.—E. T. BAILEY, M.B., F.R.C.S.                                     | 278 |
| Osteochondritis Right Talus.—E. T. BAILEY, M.B., F.R.C.S.                                                   | 279 |
| Ununited Nine-Year-Old Fracture of the Mid-Shaft of the Femur.—G. J. WALLEY, F.R.C.S.                       | 279 |
| Elephantiasis Nervorum.—PAUL MARCHAND, M.B. Witwatersrand, F.R.C.S.                                         | 281 |

(N.B.—The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.)

All communications concerning Editorial Business should be addressed to  
THE HONORARY EDITORS, 1, WIMPOLE STREET, LONDON, W.1

Applications for advertisement space in the "Proceedings" should be made to the Society's official advertising agents, Messrs. C. Mitchell & Co. Ltd., Mitchell House, 1 and 2, Snow Hill, London, E.C.1.

Copies of the whole *Proceedings* may be purchased through any bookseller. Prices are as follows:—

|                                                                  |                           |
|------------------------------------------------------------------|---------------------------|
| Single copies                                                    | 10s. 6d. each, post free. |
| Annual subscription, covering 12 monthly issues and annual index | £6 6s. 0d.                |

Reprints of Sectional parts may be obtained direct from the Society. Prices are as follows:—

|                     |                          |
|---------------------|--------------------------|
| Single copies       | 3s. 6d. each, post free. |
| Annual subscription | 15s. 0d.                 |

Fellows and Members of the Royal Society of Medicine are asked to apply direct to the Society for any copies of the *Proceedings* they may require, whether whole or Sectional, in addition to those they receive *gratis*. Prices are as follows:—

Whole *Proceedings*:

|                                                      |                          |
|------------------------------------------------------|--------------------------|
| Single copies                                        | 7s. 6d. each, post free. |
| Complete volume (12 monthly issues and annual index) | £5 0s. 0d.               |

Sectional *Proceedings*:

|                     |                          |
|---------------------|--------------------------|
| Single copies       | 3s. 0d. each, post free. |
| Annual subscription | 10s. 0d.                 |

## Section of Comparative Medicine

President—Professor WILSON SMITH, M.D., F.R.S.

[December 15, 1948]

### DISCUSSION: LIVER DAMAGE OF METABOLIC ORIGIN

Professor H. P. Himsworth: *Dietetic Lesions of the Liver in Animals.*

It is now securely established that two distinct, morphological, hepatic lesions can be produced in rats by deficient diets. The one leads from fatty infiltration, by the insidious and uniform development of fibrosis between the vascular tracts, to a diffuse hepatic fibrosis indistinguishable from Laennec's portal cirrhosis; the other arises as a sudden massive necrosis, irregularly distributed in the liver, and leads to a deeply scarred organ with marked nodular hyperplasia of the remaining parenchyma (Himsworth and Glynn, 1944).

Post-infiltrative diffuse hepatic fibrosis has been produced in dogs (Chaikoff *et al.*, 1943), rabbits (Rich and Hamilton, 1940), rats (Blumberg and Grady, 1942; Webster, 1942; Himsworth and Glynn, 1944) and probably in guinea-pigs (Spellberg *et al.*, 1942). It also occurs under several conditions in man (Himsworth, 1947). In every case it has developed on the basis of heavy, prolonged, fatty infiltration and measures which prevent this infiltration prevent the lesion. Broadly speaking, fatty infiltration may arise from an excess of dietary fat or a deficiency of those factors—lipotropic factors—which prevent fat accumulating in the liver (Best and Lucas, 1943). Diets containing a sufficient excess of fat are unlikely to occur outside the experimental laboratory, but diets deficient in lipotropic factors occur naturally. The best-known lipotropic factors are substances capable of donating methyl groups (Du Vigneaud, 1942–43). Of these the two most important are the base, choline, and the amino-acid, methionine. In consequence diets rich in choline, in protein, or in both, prevent fatty infiltration and its sequel, diffuse hepatic fibrosis. It is in just these substances that poor diets are most deficient.

Fatty infiltration is normally regarded, in itself, as an innocuous condition; but recent work indicates that it is not so. Livers which are the seat of its sequel, diffuse fibrosis, contain an excess of water and protein. Qualitatively similar changes are detectable in the fatty liver long before there is any evidence of fibrosis (Himsworth and Lindan, 1948). Similarly fatty, like diffusely fibrotic, livers have an impaired capacity to destroy certain hormones (Stephens *et al.*, 1947). Thus diffuse hepatic fibrosis seems but the final stage of a smooth sequence from fatty infiltration, rather than a new process. It would, however, be a mistake to regard the noxious effects of such infiltration as a specific property of fat. Similar sequences develop after chronic infiltration with cholesterol, kerosin, glycogen, and even metabolically inert substances such as polyvinyl alcohols; in fact diffuse hepatic fibrosis appears to be the response to chronic infiltration, irrespective of its chemical nature. It is known that heavy infiltration materially impairs the circulation through the hepatic lobules and it has been suggested that as a consequence the liver cells become malnourished, quietly die, and are replaced by fibrosis (Himsworth, 1947). It is also possible that infiltration impairs lymphatic drainage from the liver and so leads to the observed accumulation of water and protein.

The sequence from acute necrosis to post-necrotic scarring and nodular hyperplasia has been definitely produced in rats (Himsworth and Glynn, 1944) and mice (Himsworth and Lindan, 1949) and it is probable, but not certain, that it has been produced in other species. This sequence is unrelated to fatty infiltration, and choline affords no protection. Weichselbaum (1935), who first produced this type of necrosis, related it to deficiency of thio-amino-acids; later the acid in question was shown to be cystine (Glynn, Himsworth and Neuberger, 1945) and more recently a relationship to tocopherol deficiency has been



demonstrated. By the end of 1945 a peculiar situation had arisen. Reputable workers, all over the world, were producing hepatic necrosis by cystine deficiency; equally reputable ones were failing to do so. In attempting to explain the variable incidence of the lesion among his own animals Gyorgy (1947) noted that it was related to the type of dietary fat and subsequently showed that the protective fats were rich in tocopherol. He then showed that tocopherol itself would protect against development of the necrosis due to cystine deficiency. Unbeknown to him Schwartz (1944) in Germany had found that tocopherol was somehow involved in the necrosis story. Application of this knowledge removed many of the discrepancies between the results of different laboratories—but not all. Even omitting tocopherol still failed to produce a high incidence of hepatic necrosis in some. Recent work (Himsworth and Lindan, 1949) suggests the reason. Sufficient stores of tocopherol can be laid down in the body, in the pre-experimental period, to protect against cystine deficiency, if the pre-experimental diet is rich in this vitamin. We seem, therefore, to be arriving at a position similar to that in respect of pellagra. Just as pellagra can be produced by deficiency of a vitamin, nicotinic acid, or of an amino-acid, tryptophan, and just as either of these substances can protect against the lesion, so dietetic hepatic necrosis can be produced by deficiency of either cystine or tocopherol and each can protect against the effects of either deficiency.

The question remains how these dietetic deficiencies lead to hepatic necrosis. Undoubtedly in many cases, and notably in man, the necrosis is commonly precipitated by a noxious agent, poison or virus, which, but for the deficiency, would have caused only a mild and recoverable lesion rather than a massive necrosis. But it appears that in animals, under experimental conditions, these deficiencies can, by themselves, produce devastating necrosis.

The exact mechanism by which cystine and tocopherol deficiencies produce their disastrous results has not yet been established but it seems to involve two factors: (1) changes in the architecture of the liver, (2) changes in intracellular metabolism. Some hours before frank necrosis occurs the parenchymal cells are grossly swollen and simultaneously the water content of the liver increases by as much as 60%. At this stage circulation through the lobules is grossly impeded. Blood is pooled in the portal tracts and in places has burst out as periportal hemorrhages. The intestinal vessels are turgid, and hemorrhage into the guts and blood-stained ascites is present. The swollen liver cells, by compressing the sinusoids, appear to have arrested the intralobular circulation so that it is only a matter of time before necrosis follows (Glynn and Himsworth, 1948; Himsworth, 1947).

The changes in metabolism consequent upon cystine and tocopherol deficiency are as yet the subject of conjecture but recent findings are so striking that it may be profitable to consider their possible significance.

Necroses of the liver can be produced in many ways but in several types an association with derangements of sulphur metabolism is beginning to emerge. Thus necrosis can be produced by deficiency of cystine, by chlorinated hydrocarbons, by poisons such as selenium, by deficiency of tocopherol, and also by gross excess of cystine. In all save the last the lesion is aggravated by deficiency, and ameliorated by sufficiency of thio-amino-acids. Cystine deficiency causes a fall in the glutathione content of the liver, which is rapidly remedied by giving this amino-acid (Leaf and Neuberger, 1947). Selenium replaces sulphur in the amino-acids of grain grown on seleniferous soil and, presumably, thereby leads to a conditioned deficiency of cystine (Moxon and Rhian, 1943). Chlorinated hydrocarbons deplete the liver of glutathione (Binet *et al.*, 1937) and readily combine with, and inactivate, the sulphhydryl groups of certain enzyme systems (Michaelis and Schubert, 1934; Quastel, 1933). Susceptibility to these poisons is increased by deficiency of thio-amino-acids (Miller and Whipple, 1942) or of tocopherol (Hove, 1948). Thus these three methods all lead to a decreased content of active sulphur compounds in the cell. It is of interest to see how this conception would apply to the association between cystine and tocopherol deficiency. In a brilliant article Hickman and Harris (1946) have reviewed the role of tocopherol in metabolism and have concluded that this strong reducing agent is probably concerned in preserving a requisite concentration within the cell of the reduced form of certain enzymes. It is conceivable that tocopherol may be concerned in maintaining the equilibrium between reduced  $-SH$  and oxidized  $S-S$  glutathione at a point in favour of the former. If this were so, deficiency of tocopherol would lead to a reduction in sulphhydryl groups similar to that produced by actual deficiency of cystine. There remains the paradox of cystine poisoning but, if the oxidized and reduced forms of glutathione constitute an oxidation-reduction potential system of the type envisaged, addition of a gross excess of the  $S-S$  form, in the shape of cystine, would be expected to upset the whole balance, with, possibly, disastrous results. Thus it is possible to account for the common result of these diverse measures by a single, if speculative, hypothesis—that a reduction of the active sulphhydryl groups within the cell, however produced, causes changes which lead to necrosis. Whether or not this conception is valid can be shown only by future work.

## REFERENCES

- BEST, C. H., and LUCAS, C. C. (1943) *Vitamins and Hormones*. New York.
- BINET, L., WELLER, G., and GONDOND, H. (1937) *C.R. Soc. Biol., Paris*, 124, 1141.
- BLUMBERG, H., and GRADY, H. G. (1942) *Arch. Path.*, 34, 1035.
- CHAIKOFF, I. L., EICHORN, K. B., CONNOR, C. L., ENTERMAN, C. (1943) *Amer. J. Path.*, 19, 9.
- DU VIGNEAUD, V. (1942-43) *Harvey Lect.*, 38, 39.
- GLYNN, L. E., and HIMSWORTH, H. P. (1948) *Clin. Sci.*, 6, 235.
- , —, and NEUBERGER, A. (1945) *Brit. J. exper. Path.*, 26, 326.
- GYORGY, P. (1947) 6th Conf. Liver Injury, Josiah Macy Jr. Foundation Rep. New York, p. 67.
- HICKMAN, K. C. D., and HARRIS, P. L. (1946) *Advances in Enzymology*, 6, 469.
- HIMSWORTH, H. P. (1947) *Lectures on the Liver and its Diseases*. Oxford.
- , and GLYNN, L. E. (1944) *Clin. Sci.*, 5, 93.
- , and LINDAN, O. (1948) Unpublished.
- , — (1949) *Nature*, 163, 30.
- HOVE, E. L. (1948) *Arch. Biochem.*, 17, 467.
- LEAF, G., and NEUBERGER, A. (1947) *Biochem. J.*, 41, xx.
- MICHAELIS, L., and SCHUBERT, M. P. (1934) *J. biol. Chem.*, 106, 331.
- MILLER, L. L., and WHIPPLE, G. H. (1942) *J. exp. Med.*, 76, 421.
- MOXON, A. L., and RHIAN, M. (1943) *Physiol. Rev.*, 23, 305.
- QUASTEL, J. H. (1933) *Nature*, 131, 206.
- RICH, A. R., and HAMILTON, J. D. (1940) *Bull. Johns Hopkins Hosp.*, 66, 185.
- SCHWARTZ, K. (1944) *Hoppe-Seyl. Z.*, 281, 101 and 109.
- SPELLBERG, M. A., KEATON, R. W., and GINSBERG, R. (1942) *Arch. Path.*, 33, 304.
- STEPHENS, L. H., and RALLI, E. P. (1947) *Endocrinology*, 41, 1.
- WEBSTER, G. (1942) *J. clin. Invest.*, 21, 285.
- WEICHELBAUM, T. E. (1935) *Quart. J. exp. Physiol.*, 25, 363.

Mr. J. D. Steel: *I. Facial Eczema in Animals.*

This condition occurs mainly in New Zealand though there are occasional reports of its occurrence in Australia. What is known of the disease has been described by Cunningham, Hopkirk, Filmer, Clare and others in the *N.Z. J. Sci. Tech.* in a series of papers beginning in 1940. Both cattle and sheep are affected, the disease being more serious in the smaller ruminant. It is characterized by liver damage, icterus and dermatitis due to photosensitization.

Facial eczema has been known in New Zealand since 1897. The disease occurs mainly in the North Island and major outbreaks were encountered in 1908, 1910, 1935 and 1938.

The incidence of the disease is seasonal. Most cases are seen in the autumn though some may be seen in the spring. There is considerable variation in incidence from year to year. As a generalization it can be said that the incidence is low except when special seasonal conditions are favourable to its development. The predisposing climatic factors are a period of summer drought, with high environmental and soil temperatures, followed by early autumn rain and the rapid regrowth of pasture. To illustrate this point—in 1938 when a major outbreak occurred, January was hot and dry and February and March were the hottest months experienced in New Zealand since records began. The pastures available for grazing were dried out and closely eaten off. When the drought was broken by rain in early April there was a rapid regrowth of grass and a high incidence of the disease. Under such conditions the morbidity may be 70-80% in sheep flocks and the mortality from 5-50%. In cattle the morbidity may be 50%, but only a few animals actually die. In sheep the young animals are more susceptible than the adult.

Two factors enter into the aetiology of facial eczema. There is a primary liver damage factor and a secondary photodynamic factor. It is the operation of the latter which draws attention to the disease, hence the term facial eczema. The nature of the process causing liver damage is unknown. The evidence points to the important liver damage occurring during the period of drought with the result that after rain the sheep has to face a rapid regrowth of pasture with a functionally inadequate liver.

Clare (1944) has described the photosensitizing agent which is phyloerythrin. This substance is a porphyrin, not preformed in herbage, but derived from chlorophyll during the passage of herbage through the alimentary tract. Thus phyloerythrin is normally present in the bile and faeces of herbivora. When a sheep with liver damage has to ingest young, rapidly growing grass the accumulation of phyloerythrin in the blood reaches a level beyond the liver's excretory capacity. At this stage the skin becomes sensitive to light and dermatitis appears.

Clinically the onset of the condition is sudden and a number of animals are affected simultaneously. Affected animals scratch and seek shade. This is followed by oedematous swelling of the ears, eyelids, face and lips—parts that are unprotected by wool from the sun. The scratching continues and is accompanied by serous exudation and crust formation. Finally there is skin necrosis and scab formation.

In cattle the dermatitis is most prominent on the udder and teats but it may occur on any area where skin pigmentation is slight.

Accompanying the dermatitis there is icterus which varies in degree and persistence. In some animals it is marked from the onset and can be detected for several weeks. In others jaundice is slight.

Many cases die within a few weeks of the onset. Others survive and pass into a chronic phase in which there is steady loss of condition and death in the winter, or there is apparent recovery with a relapse in the following spring or autumn. The onset of cold, dull weather hastens the disappearance of the dermatitis.

At autopsy there is generalized icterus of variable intensity. The peritoneal cavity contains a yellow fluid and the urine is dark yellow. The most important changes are found in the liver. There is fine mottling or irregular blotching of both lobes and these changes extend into the liver substance. The left lobe of the liver is atrophied and the margin is contracted and fibrous. The large intrahepatic bile ducts have thickened, fibrous walls. In long-standing cases there may be almost complete atrophy of the left lobe with areas of regeneration in the right lobe causing a compensatory hypertrophy.

Histologically the portal area is said to be the chief site of damage. The changes described are fibrosis and bile-duct proliferation. The fibrous tissue is said to surround the lobules and cause pressure necrosis. The damage is not regular over the whole liver, the left lobe showing extreme damage and the right lobe mild lesions.

#### BIBLIOGRAPHY

- CLARE, N. T. (1944) *N.Z. J. Sci. Tech.*, 25, 202A.  
 COOPER, E. R., and WALKER, D. (1940) *N.Z. J. Sci. Tech.*, 22, 30A.  
 CUNNINGHAM, I. J., HOPKIRK, C. S. M., and FILMER, J. F. (1942) *N.Z. J. Sci. Tech.*, 24, 185A.  
 LEVY, E. B., and SMALLFIELD, P. W. (1942) *N.Z. J. Sci. Tech.*, 24, 198A.

#### [II. *Enzootic Jaundice of Sheep*

This disease occurs in Australia and it was first described as a distinct entity by Albiston in 1929. Further papers by Albiston *et al.* (1940) and Edgar *et al.* (1941) have defined the syndrome more clearly and reported the results of early investigations. Since this time three reports have been published by the investigation committee on enzootic jaundice which was set up in 1938.

The disease is characterized clinically by icterus, anæmia and hæmoglobinuria and pathologically by liver damage.

Sheep are the only species affected but there are differences in breed susceptibility. The disease is mainly confined to British breeds and their crosses, Merino sheep being only rarely affected.

Most outbreaks of enzootic jaundice have occurred in relatively restricted areas of N.S.W. and Victoria. There is a close correlation between the incidence of the disease and the age of the sheep. The mortality is greatest in animals 3 or more years old and may reach 30% per annum. Both sexes are equally susceptible. Deaths are likely to occur at two periods of the year, viz. autumn and early winter (April-July) and late spring and early summer (October-December).

The ætiology of enzootic jaundice is obscure and the only way of giving a picture of some of the factors involved is by tracing the history of the theories put forward to explain its occurrence. The first suggestion, made by Rose and Edgar in 1936, was that the disease was an enterotoxæmia caused by *Cl. welchii*, type A. When this view could not be substantiated the similarity between the naturally occurring disease and experimental chronic copper poisoning was noted. This led to an extensive investigation of the possible role of copper in the ætiology. The first investigations on the copper theory were encouraging. These studies showed that under pastoral conditions favourable to the development of the disease large amounts of copper accumulated in the liver and in animals dying of the disease the concentration of copper was very high. It was also shown that just prior to the onset of clinical jaundice there was a rise in the blood copper of short duration. About twenty-four hours after the rise in blood copper there was a hæmolytic crisis with a marked fall in the erythrocyte count, hæmoglobinæmia and hæmoglobinuria. Despite these apparent leads the observations did not fit all the facts. Liver copper values were extremely variable and the disease occurred in some animals whose copper status was normal. However, since the majority of affected sheep had a high copper status an attempt was made to control the accumulation of copper in the liver by providing an iron sulphide lick. This experiment was inconclusive and was followed by an experiment designed to test the effect of plane of nutrition on the incidence of the disease. The evidence obtained indicated that a high plane of nutrition delayed the onset of the disease but did not prevent it.

Concurrent studies of pasture conditions indicated that when the season favoured the growth of grass rather than herbage a high copper status in the liver was not produced. Since *Heliotropium europaeum* had been suggested as the offending herbage and as it was widely distributed in the enzootic areas an experiment was designed to test the effect of controlled grazing on heliotrope. Using approximately 250 sheep in two groups there was a 41% mortality in the group having access to heliotrope and an 11% mortality in the non-heliotrope group over a period of thirteen months. Heliotrope has a high mineral content, including copper, and it was thought that the ingestion of this plant might help to raise the copper status of the sheep. At the conclusion of the heliotrope-grazing experiment all the surviving sheep were slaughtered and their liver copper values were estimated. A wide range of copper values were found and there was no significant difference between the two groups. The importance of heliotrope-grazing on the aetiology of enzootic jaundice received a setback in 1946 when, after a wet summer and an excellent growing season, severe outbreaks of the disease occurred on pastures dominated by subterranean clover. Recent studies on the possible role of molybdenum in controlling the copper status of both plant and animal have not as yet yielded conclusive results.

To summarize, enzootic jaundice is associated with a high copper concentration in the livers of the majority of affected sheep. A high plane of nutrition delays but does not prevent the occurrence of the disease. Finally, grazing on heliotrope is associated with a higher incidence than when access to this plant is restricted.

The clinical signs of enzootic jaundice are difficult to integrate into a clear picture. As originally described the disease was characterized by icterus, anaemia, haemoglobinuria, loss of condition, prostration and death. Since that time an appreciable number of cases have occurred in which the so-called haemolytic crisis was not present. Whether this indicates the existence of more than one syndrome cannot be decided at present.

At autopsy affected sheep show generalized icterus of variable intensity. The liver may be greatly enlarged and its colour is markedly altered varying from a bright ochre to a dull brown. The liver shows fatty infiltration and diffuse fibrosis. From the evidence available it is impossible to give definite information on the presence or absence of centrilobular necrosis. It is mentioned, but only vaguely and chiefly in connexion with a hypothesis relating to the toxicity of copper. The liver may contain up to 40% fat when calculated on a fresh-wet-weight basis. Diffuse fibrosis may be detected macroscopically. In the heliotrope-grazing experiment mentioned previously 34% of the sheep that were grazing on heliotrope and were sent for slaughter at the termination of the investigation showed diffuse hepatic fibrosis discernible macroscopically.

#### BIBLIOGRAPHY

- ALBISTON, H. E. (1929) *Aust. vet. J.*, 5, 26.  
 —, BULL, L. B., DICK, A. T., and KEAST, J. C. (1940) *Aust. vet. J.*, 16, 233.  
 EDGAR, G., HINDMARSH, W. L., KEAST, J. C., and ROSE, A. L. (1941) *Aust. vet. J.*, 17, 120.  
 Rep. Invest. Comm. on Toxic Jaundice (1944) *Aust. vet. J.*, 20, 265; (1947) 23, 38 and 253.  
 ROSE, A. L., and EDGAR, G. (1936) *Aust. vet. J.*, 12, 212.

#### III. KIMBERLEY HORSE DISEASE OR WALK-ABOUT DISEASE

This condition was described by Murnane and Ewart in 1928. Though not quite so pertinent to the experimental work Professor Himsworth has described, it raises an interesting issue, namely the relation of liver damage to involvement of the central nervous system.

The disease occurs in the Kimberley district of Western Australia where it has been known for sixty years. It has been reported in the Northern Territory and its occurrence suggested in Queensland.

There is a distinct seasonal incidence from January to April each year, the appearance usually coinciding with the onset of the "wet" season. Horses of all ages and sex are susceptible and on some properties the annual morbidity is 25%.

The clinical signs are anorexia, dullness, voluntary segregation from other horses and a sleepy attitude. The affected horse stands in a corner of the yard or under a tree with the head down as if sleeping. Periodically the animal rouses itself and moves about grazing but soon it again assumes the sleepy attitude. This is followed by progressive wasting leading to emaciation and irritability exhibited by biting other horses, gnawing at posts, the bark of trees or leather straps. The appetite becomes depraved and filth and refuse may be eaten. Yawning is a marked and almost constant sign at the onset of the disease. Subsequently, muscular spasms occur and these are followed by a sudden phase of mad galloping in which the horse has no sense of direction and is uncontrollable. This phase is transient but it can be precipitated by suddenly startling the resting animal. The attacks of unrestrained galloping become more frequent but less violent and gradually they merge

into the walking stage. At this time constant walking with a slow, staggering gait and a low, stiff carriage of the head is the most striking feature.

Dysphagia and drooling are often noticed. An affected horse may walk about for hours with a mouthful of unchewed grass protruding from its lips. The horse will walk quite stupidly into fences, trees, rivers or any object in its path. Should progress be blocked by a fence the animal will remain obstinately pushing against it with great force. In time this leads to traumatic injury to the head, body or legs. Dilatation of the pupil, blindness and the assumption of abnormal postures such as crossing the fore-legs are observed. In the early stages the cardinal signs are normal. In the terminal stages the temperature is raised ( $103\text{--}4^{\circ}\text{F.}$ ), the respiration increased and the pulse rapid.

Other signs are œdema of the limbs and head and just before death icterus and hæmoglobinuria may develop.

The outstanding pathological finding is liver damage. There is marked cirrhosis both within and around the lobule but chiefly in the perilobular site. Small hæmorrhages into the liver substance are also found. There is ascites and œdema of the limbs and intestines. There is no evidence that the central nervous system has ever been examined.

Kimberley horse disease is due to the ingestion of *Atalaya hemiglaucæ* or whitewood, a small shrub which is eaten voluntarily by horses and is often fed to them when food is scarce. The disease can be produced experimentally by feeding horses on whitewood for about three months. In 1931 Ewart described the toxic principle in whitewood as a saponin. No satisfactory treatment for Kimberley horse disease is known but it is readily prevented by not allowing access to the poisonous shrub.

Australia is not the only country where equine diseases characterized by liver damage and signs of nervous involvement occur. Similar diseases have been reported from New Zealand, South Africa, and North America. The poisonous plants incriminated in most of these countries are various species of *Senecio* or Ragwort.

In 1912 Wilson described a disease in man known as hepatolenticular degeneration. There are many similarities between the equine disease just described and human hepatolenticular degeneration. While the ætiology of the two diseases may not be the same it seems reasonable to suggest that a reinvestigation of the equine disease might be profitable.

Evidence has been presented for the occurrence in herbivora of liver damage in which nutritional and metabolic factors play an important part. In selection of material for this Discussion I have sought naturally occurring diseases presenting features that may have their analogy in the types of liver damage described in the rat by Himsworth, Glynn and others.

#### BIBLIOGRAPHY

- EWART, A. J. (1931) *Bull. Coun. sci. industr. Res. Aust.*, No. 50, p. 28.  
MURNANE, D., and EWART, A. J. (1928) *Bull. Coun. sci. industr. Res. Aust.*, No. 36, pp. 61.  
WILSON, S. A. K. (1912) *Brain*, 34, 296.

Professor H. P. Himsworth in reply to the subsequent discussion:

Several speakers have remarked that in the diseased livers of animals suffering from various conditions, the pathological process is often more advanced in one-half of the organ. This phenomenon occurs in man and experimental animals. The left lobe supports the brunt of the attack. In the severest cases it is reduced to a fibrous leaf. In the less severe the regeneration nodules are bigger here so that the left lobe may be actually larger than the right. The two halves of the liver receive blood from different parts of the portal tract; the right from the small intestine, the left from the spleen and large intestine. In dietary deficiency, therefore, the left lobes become depleted earlier and more severely. The finding of a difference in severity between the two lobes is an indication that nutritional factors may play a causative, or predisposing, role in the production of the lesion.

It has been asked why diffuse hepatic fibrosis does not develop in the grossly fatty livers of hibernating animals. The explanation seems to be that the metabolic rate is a determining factor. After thyroidectomy diffuse hepatic fibrosis does not develop in the presence of fatty infiltration of a degree which readily causes this lesion in normal animals. If, as has been suggested, infiltration produces its deleterious effects by retarding the intralobular circulation and so allowing the blood to be deprived of its nutriment before it has completely traversed the sinusoids, it can be seen that when the metabolic rate is low the requirements of the parenchyma will be less, the slowly percolating blood will be less rapidly depleted, and so the reduced needs of the parenchymal cells will be met even in the distant centrilobular zone.

# Section of Epidemiology and State Medicine

President—Sir ALLEN DALEY, M.D., F.R.C.P., D.P.H., K.H.P.

[November 1, 1948]

## DISCUSSION ON THE PREVENTION OF ACCIDENTS

Mr. William Gissane: From an experience based on the hospital treatment of all types of injury due to accident, certain observations may be made.

The first is that accidents outnumber by approximately ten to one the combined medical and surgical emergencies received into the casualty department of any busy general hospital. In a national survey it was found that 1,318 hospitals received over one and a quarter million accidents in 1935.

The second observation, having regard to this huge number of accidents, is that the usual hospital facilities for the reception of accidents are totally inadequate.

The third observation is that the events leading up to accidents, as recounted by the victims, have their roots in very human and everyday matters; particularly is this so in home accidents, and road accidents in children. For example, a large proportion of the national accident total is made up of home accidents of a domestic type, and 60% of these are caused by falls in and around the home. The commonplace causes of these falls are readily available from the victim, and the study of such information may well lead to practical methods of home accident prevention by education through personal contact. Further, industrial injuries, as I have observed them, are much more frequent in jobs that do not demand much thought from the worker, where the machines, for example small power presses, are planned to do the thinking part of the work. On the other hand, really dangerous-looking jobs such as work in heavy stamp shops and in foundries, which demand full concentration by the worker upon the job at hand, are notable for the relative infrequency of accidents. The study at hospital level of the human factor in accident prevention may bear fruit.

The fourth observation is very soundly based. If surgical knowledge won during the last two decades be made available to the victim of every accident, much can be prevented in human suffering, permanent disability and prolonged illness.

These observations lead to some conclusions. The overriding conclusion is that if we are to tackle accident prevention in its widest field we need first to pay proper attention to the accident problem at hospital level.

We need a new type of organization within our hospitals for the adequate treatment and the adequate study of the whole accident problem, including accident prevention.

*Staffing.*—First it is necessary to attract more senior medical men to our accident services, for any improvement in our present service must be based upon the principle that surgeons of mature judgment shall be available to examine, to treat, and particularly to take a truly comprehensive view of every accident. This is important in every serious accident, and serious accidents are those likely to result in permanent disability. Once an accident was judged as serious only when life was in jeopardy. Now the restoration of the victim to normality, the prevention of preventable deformity, the resettlement of the victim to normal domestic and occupational environment with a real appreciation of time, is the objective. All this requires a new standard of assessment and treatment, and a new standard of hospital organization.

Informed opinion has accepted the necessity for such a reorganization within our hospital services, but some still express doubt on the necessary capital cost of such a reorganization. The present cost of accidents has been assessed at £250 millions a year. It is reasonable to expect that an over-all economy in this cost can only be made by reorganizing the hospital service so that each victim of an accident shall have the best primary treatment and over-all assessment modern surgery can offer. This can be effected not only by concentrating the treatment of accidents to fewer hospitals, but also by having in each good facilities and adequate staffs capable of taking the essential over-all responsibility in the care of each patient. At present we scatter one and a quarter million accidents over 1,318 hospitals, an organization which must be expensive and is known to be inadequate.

The training of efficient accident surgeons is the first need. That phase has commenced and is known to be a practical and technically attractive proposition, but from the numbers of patients requiring urgent treatment it is a very hard-worked life for the surgeon. Therefore it is essential that the facilities within our hospitals be reorganized to enable accident services to work smoothly and efficiently, having regard to the numbers of patients demanding treatment. The Delevine Committee recognized the necessity for reorganization in 1939 after a

national survey. The need now requires confirmation at a high level in the new Health Service. If the need is reaffirmed, and proper facilities are allowed, then medical men of the right calibre will be attracted to accident services.

*The plan of hospital units.*—In the reorganization of facilities, the first essential concerns the reception of casualties to hospitals. At that stage matters can become chaotic so that the first thorough, quiet examination and over-all assessment of the victim cannot be made. Through education, the public is now aware of the potential seriousness of relatively minor injuries, and seeks hospital treatment for common cuts, abrasions, lacerations, and minor fractures. These injuries are important and if neglected or poorly treated are often responsible for unnecessarily prolonged disabilities. On a national scale we know that infections of minor wounds of the hands are a major problem, are, in fact, the most expensive single item in the over-all cost of industrial accidents. In these days infection of such wounds can be prevented by adequate dressing techniques. In a busy admission department of a hospital, such injuries are responsible for over 50% of the total new accidents. If special facilities are not provided for their reception and expeditious treatment the numbers can seriously disturb the smooth working of the admission department as a whole. Further, some of these apparently trivial injuries are, in fact, serious accidents. A small skin wound on a finger is not infrequently associated with the division of digital nerves and flexor tendons and the prompt recognition and the expert treatment of such an injury may well save a precision worker to precision work. Inadequate treatment may alternatively require the expensive re-training of a disabled worker.

To prevent disabilities from these types of injury, the first examination of all minor injuries must be in the hands of a competent medical man, and, for the expeditious disposal of the large numbers of such patients, dressing stations for the injuries and operative facilities for those wounds requiring surgery should be available on the spot.

In the plan of an ideal, very large, accident admission department, the suite for the reception and treatment of these patients is centrally placed. Beside this self-contained suite is a department for the treatment of "stretcher casualties" made up of fractures, of injuries to the lower extremity and the back and of more serious injuries to the upper extremity. This is also a self-contained suite comprising examination room, waiting room, X-ray facilities, fracture theatre and plaster room, and a post-operative waiting room before disposal of the patients to out-patient treatment.

These two suites receive in a large accident centre approximately 98% of the volume of each day's new patients. The traffic through each is extremely busy, and each provides a real twenty-four-hour service.

Injuries so severe as to place life in immediate jeopardy require very special consideration. Accidents are responsible for approximately 20,000 deaths each year. Some of these deaths can be prevented by improved treatment facilities within hospitals. It is now known that all unnecessary movement of a severely shocked patient is extremely dangerous. Full treatment facilities must therefore be built around this particular problem and it should be physically segregated from the rest of the busy admission department.

*Rehabilitation.*—In the treatment of an injury from accident it is essential to correlate the initial surgical treatment with a definite plan for the restoration of the patient to his pre-accident activities and occupation. For this reason accident services require rehabilitation facilities and these should be available on a much more extensive scale than is usually recognized in hospital practice.

This point is best illustrated by an example of good technical surgery and poor over-all planning. A young ex-soldier was recently transferred to us from a Government Retraining Centre two and a half years after he had received a through-and-through wound of his right wrist. The aim of surgery had been to restore a mobile right wrist and the functional result would have been most useful to a professional violinist. Yet before the war this man had been a bricklayer's mate and desired to continue working in the building trade. At the end of surgery he was sent to a Government Training Centre to be trained as a bricklayer. After an initial four weeks' theoretical course he was required to pick up a brick. For the first time the wrist was found permanently incapable of such heavy work.

For the prevention of such expensive surgical mistakes provision must be made in hospitals for a rehabilitation department to test the results of surgical treatment against the occupational requirements of the patient.

*Regional planning.*—By planning it is possible so to arrange the accident services for a region that a large central accident department can well serve a large densely populated area. In practice, the very large numbers of relatively minor injuries can well continue to be treated in the outlying hospitals, and a great deal of out-patient after-care work should continue to be carried out near the homes of the accident victims. Yet every serious accident in this thickly populated island could be within reasonable transport distance of a hospital

where treatment of the highest order could be available for all accidents on a twenty-four-hour service.

For nearly twelve months in Birmingham we have had practical experience of using a Mobile Surgical Unit carrying its own equipment and surgical staff to serve outlying hospitals and general practitioners faced with the first care of the seriously injured. Undoubtedly this unit has saved many lives, and has proved that it is possible to link up outlying hospitals with a centrally placed full accident service.

If we are to pursue the accident problem in a practical manner we should first accept it as it is and aim to prevent the preventable results of accidents. But in addition, at hospital level, we should pursue the problem of accident prevention from the human angle by education through personal contact with the victims and their families.

**Dr. L. Colebrook:** The Annual Reports of the Registrar-General for the first thirty-nine years of this century, that is up to the beginning of the Second World War, show that no less than 78,911 persons died as a result of burns and scalds in England and Wales—an average of 2,000 a year. Very few of these deaths were the result of enemy action (during World War I): they were nearly all attributable to the usual hazards of civilian life.

No figure can be given for the non-fatal accidents during the same period: it would depend upon the severity of the injury which was included. But on a rough estimate it is safe to say that the number of persons suffering from burns and scalds severe enough to require treatment in hospital was not less than 10 times the number of fatalities, i.e. 789,000 for the 39 years, or 20,000 a year. That is almost certainly an underestimate, and it leaves out of account the legacy of misery which these injuries have so often imposed on the victims.

The Registrar-General's returns bring out several points of interest: (1) The number of deaths a year has fallen from about 2,500 a year at the beginning of the century to about 1,200 in 1939. How far that fall has been due to a reduction in the number of accidents, and how far to better treatment of the injuries, is not clear. Certainly better treatment has played a part; and also I have no doubt, the remarkable decline in virulence of the hæmolytic streptococci which has occurred all over the world in the past forty years. Although the literature of burns has little evidence on the point there can be no doubt that these microbes were responsible for a large proportion of the deaths in the past. (2) About 50% of the deaths in the whole period have occurred in children, but this proportion has not been constant. At the end of the last century it was over 70%; since then it has steadily declined till in 1939 it was only 43%. The total deaths of children under 5 years of age have always been much higher than those of older children. (3) The number of deaths among old people, i.e. over 65, has steadily increased—from about 200 a year at the beginning of the century to about 350 in 1939. Here again it is not clear that the accident rate has changed; it seems probable that the increase has been largely due to the greater number of old people at risk.

When we enquire into the circumstances in which these too-numerous accidents have happened the Registrar-General's returns are not very helpful, for, although he has for many years attempted to break down the deaths into categories, e.g. "flannelette", "playing with fire", "falling into fire", "molten metal", &c., there is always a very large proportion of them which evidently could not be classified because the certificates did not give the necessary data. This residue of cases classed as "otherwise or not stated" has often amounted to nearly 50%.

The literature of burns—amounting to something like 2,000 papers catalogued—is also not very informative on this aspect of the problem. Few authors have produced data calculated to rouse public opinion, or have voiced the view that a serious drive was needed to reduce the number of accidents.

This dearth of information probably is due in turn to the scantiness of hospital records about burns and scalds. These injuries have been received in comparatively small numbers in every general hospital (where they were never very welcome) and in few have they been made the subject of serious study prior to the Second World War.

The establishment in 1944 of the Medical Research Council Burns Unit at the Birmingham Accident Hospital (with the help of a grant from the Bernhard Baron Trust) has given opportunity for an enquiry to be begun into the factors associated with these accidents. During 1945-47, 736 cases were treated as in-patients in the Unit. (These, by the way, were only about half of the cases requiring admission to hospital in the Birmingham area—the remainder were treated in the other hospitals.)

The first point which arises from an analysis of these 736 cases<sup>1</sup> is that two-thirds of the

<sup>1</sup> I am indebted to my wife for much of the work entailed in this analysis.



accidents had occurred in or about the home, and only one-third at the individual's place of work—in spite of the fact that Birmingham is a highly industrialized city (Table I).

TABLE I.—RELATION OF THE ACCIDENTS TO INDUSTRIAL WORK OR HOME HAZARDS (M.R.C. BURNS UNIT.)

|                                 | Cases        | Deaths | Case mortality % |
|---------------------------------|--------------|--------|------------------|
| Industrial (ages 15-79) .. .. . | 232<br>(32%) | 3      | 1.3              |
| Home (all ages) .. .. .         | 504<br>(68%) | 36     | 7.1              |
| Total                           | 736          |        |                  |

At first sight that would suggest that the hazards of the home are much greater than those of industry but it is doubtful whether that conclusion would be justified. For it must be remembered that the burns at home represent all age-groups, whereas those occurring in industry are almost entirely confined to the age-group 15 to 70. Enquiry from Dr. Percy Stocks elicited the fact that the persons "at work" represent 42% of the total population. But how many of the 42% are exposed to special risk of burns and scalds by virtue of their occupation is probably not known. I imagine it is not likely to be more than one-half. On that supposition only 21% of the population are exposed to special risk in industry. Since 32% of our admissions were industrial burns and scalds it may be that the risks of industry are in fact a little higher than those of the homes. (Women doing housework do not, I gather, come into the category "at work".)

It may be noted in passing that the mortality rate (Table I) of the industrial accidents in our series has been very much lower than that of the home accidents. This is due in part to the fact that a large number of the industrial cases had comparatively small burns, produced by molten metal; and in part to the fact that many of those injured at home were extensively burned by their clothes catching fire—and often they were old people, among whom the mortality rate after burning is notoriously high.

The second feature which emerges is the striking disproportion in the age-groups—and sometimes also in the sex—affected by these accidents. Table II shows that:

TABLE II.—DISTRIBUTION BY AGE AND SEX OF 504 HOME BURNS AND SCALDS (WITH MORTALITY)

|        |       | 0-5 |    | 5-14<br>(inc.) |    | 15-64<br>(inc.) |    | 65<br>+ | All<br>ages |     | Deaths<br>(all ages) |    |
|--------|-------|-----|----|----------------|----|-----------------|----|---------|-------------|-----|----------------------|----|
|        |       | M.  | F. | M.             | F. | M.              | F. | M.      | M.          | F.  | M.                   | F. |
| Burns  | .. .. | 38  | 48 | 29             | 20 | 41              | 44 | 2       | 110         | 135 | 3                    | 30 |
| Scalds | .. .. | 104 | 64 | 20             | 18 | 13              | 31 | 1       | 138         | 121 | 0                    | 3  |
|        |       | 135 |    |                |    | 110             |    |         | 245         |     |                      |    |
|        |       | 206 |    |                |    | 53              |    |         | 259         |     |                      |    |

(a) Of the combined burns and scalds occurring at home no less than 50% happened to children under 5 years of age, and 67% if we include the older children.

(b) Of the 259 scalds no less than 168 (65%) occurred in children under 5. There were four times as many in this group as in the older children.

(c) The incidence of scalds was decidedly higher among boys than among girls (124 to 82). Presumably the boys were more inclined to investigate teapots, saucepans, &c.

(d) The incidence of burns was somewhat higher among girls under 5 than among boys of the same age. (This difference is shown still more definitely in the Registrar-General's returns of deaths.) The greater tendency for girls' frocks to catch fire (especially when they are of inflammable cotton material such as flannelette and winceyette) is no doubt responsible for these differences.

(e) Both burns and scalds occurred much more frequently among the older women than among the men of the same age-group (31 to 3).

(f) The mortality was also much higher among the females than the males (33 to 3). It was also much higher for burns than for scalds.

The third point brought out by our analysis is the importance of epilepsy as a factor in the causation of burns (Table III). In 25% of the adults burned at home the accident had

occurred during a fit—and in all these cases the history of epilepsy was definite. A few more patients gave an indefinite story of having been burned during a "turn" or a fainting fit but these have not been included in Table III. It seems probable that some epileptics are

TABLE III.—EPILEPSY AS A FACTOR AMONG THE 110 ADULT HOME BURNS

|                     | Cases | Deaths | Case mortality % |
|---------------------|-------|--------|------------------|
| Epileptic .. .. .   | 27    | 7      | 26               |
| Other burns .. .. . | 83    | 18     | 22               |

not taking precautions in the homes, e.g. by the constant use of fireguards, because they do not wish to call attention to their condition. The injuries they sustain from burning accidents are apt to be particularly severe because they lie on the fire long enough for very deep burning to occur. Thus two women in this category with burns of the head and face have already occupied hospital beds for 278 and 222 days respectively—and both of them still require considerable plastic repairs.

### *The Nature of the Accidents*

The 232 industrial accidents have not been investigated in any detail, but there is no doubt that the largest single factor was the splashing and spluttering of molten metal.

The nature of the 504 home accidents is summarized in Tables IV and V. Table IV shows

TABLE IV.—ANALYSIS OF 245 HOME ACCIDENTS CAUSING BURNS

|                                                            |     |
|------------------------------------------------------------|-----|
| <i>Clothes caught fire or patient fell on fire</i> .. .. . | 118 |
| Coal fire .. .. .                                          | 67  |
| Electric .. .. .                                           | 30  |
| Gas .. .. .                                                | 12  |
| Not specified .. .. .                                      | 9   |
| <i>Other causes</i> .. .. .                                | 127 |
| Inflammable liquids .. .. .                                | 22  |
| Bonfires .. .. .                                           | 11  |
| Hot fat .. .. .                                            | 11  |
| Electrical equipment .. .. .                               | 9   |
| Matches .. .. .                                            | 6   |
| Gas oven .. .. .                                           | 5   |
| Hot metal .. .. .                                          | 5   |
| Conflagrations .. .. .                                     | 2   |
| Various .. .. .                                            | 56  |

TABLE V.—ANALYSIS OF 259 HOME SCALDS

|                               |    |
|-------------------------------|----|
| Teapots and teacups .. .. .   | 68 |
| Other hot liquids .. .. .     | 81 |
| Baths left unattended .. .. . | 26 |
| Various other causes .. .. .  | 77 |
| Not known .. .. .             | 7  |

259

that almost 50% of the burns resulted from clothes catching fire or from the patients falling on to a fire. Open coal fires were involved in 67 instances. In 60 cases no guard was in use: only one of the remaining 7 patients was an adult—an epileptic woman who fell over a low guard in a fit. All the rest were children under 5. One jumped over the guard; two others were left alone with a guarded fire and somehow contrived to get burned; another sat on a hot guard; the remaining two ignited paper or rag and set their clothes on fire.

The increasing number of accidents associated with electric radiants is noteworthy. 29 of the 30 had no guard beyond the occasional bars which are put across to protect the elements but do not prevent a frock or nightdress touching them. In the one home where a guard was generally used with the radiant it had been removed at the time of the accident.

Among the accidents listed as due to "other causes" it is worthy of notice that (a) only 9 were ascribed to electrical equipment, (b) 11 were associated with bonfires or fireworks, (c) only 2 were caused by a conflagration—and neither of them was fatal. The low incidence of accidents of this type in our series is in agreement with the Registrar-General's returns of peacetime years, where only about 3% of the total deaths have been associated with a conflagration. This point is made because it is sometimes said that a complete census of burns and scalds could be prepared from the records of the Police and National Fire Services. In fact neither of these Services was cognizant of many of the accidents for which patients were admitted to the Burns Unit.

Table V summarizes the 259 scalding accidents which occurred in the home. It is apparent that the upsetting of teapots and teacups was the largest single factor—accounting for approximately 25%. Enquiries of the parents of many of these scalded children have made it abundantly clear that a large proportion of the accidents was due, in the last resort, to a lack of awareness of danger on the part of those in charge of the children: teacups and teapots were put down within their reach; saucepans were put on the fire or the stove with the handles easily accessible; a bath of hot water was left while the mother went to fetch some cold water or the soap, &c. Also, many parents did not realize that tea which had been made ten minutes before might still be hot enough to scald the tender skin of a young child, especially if it soaked his clothing.

Those are the chief findings in our preliminary study of this problem. Briefly they amount to this: that there are far more serious burns and scalds occurring in the homes than in industry; that the most serious of these home burns are those of children, old people and epileptics; and that many of the home burns and scalds accidents were of such a kind that they could have been prevented by reasonable care and foresight. By this I mean that if the guarding of coal, electric and gas fires had been habitual instead of exceptional, and if greater caution had been used in the handling and disposal of hot liquids, most of the accidents would not have happened.

### *Prevention of the Accidents*

*Burns.*—The hazards of the home will continue to be numerous so long as we use open coal fires and unguarded electric and gas radiants to heat our houses and to cook our food. In the future perhaps the development of district heating and of electric power for cooking will replace these dangerous appliances in the most dense centres of population. In the meantime we could and should take steps to protect at least the children and old people and the epileptics (whose injuries comprise 76% of all the home burns). The old-fashioned fireguard has proved an unsatisfactory solution for the problem of the open fire: it has to be removed for stoking the fire and for cooking, and, since it gets in the way, is often discarded altogether. It would make for greater safety and be less easily removed by children if it was always hooked on to a staple in the wall but I am informed that in some Council houses the tenants are not allowed to put in such a staple. In new houses a built-in guard on the lines suggested recently by a Birmingham architect (Mr. Worthington) could be provided, and should make for safety. This is designed to slide in and out as required, one panel on either side of the grate and another above it, and to be latched or padlocked when in position in front of the fire.

The problem of electric and gas fires could be solved much more easily if we had the will to do so. Many of these heaters are especially dangerous because they can be moved about the house and, being light, are readily upset. The great majority of accidents associated with them are due to a momentary contact of an inflammable garment with the naked element. A light guard fixed at 3 inches or more from the element would prevent this direct contact. The garment would not catch fire even after several minutes' contact with the guard although it might scorch (and in that way would usually give warning of danger). In several countries, notably Australia, Denmark, Iceland and, I think, some of the Canadian provinces, no electric fire may be sold which does not carry a fixed guard conforming to specific safety regulations. In this country we protect the public against the sale of poisons, against adulterated food and the indiscriminate use of firearms. Why should we not protect them too against the much more common danger associated with the use of electric and gas fires in the home?

It may be argued that at the Birmingham Accident Hospital there were only 30 burns from electric fires in three years. Admittedly the number is not large, but 7 of the victims died, and of those who survived, several children will have terribly disfigured bodies for the rest of their lives. Two of them were in hospital for 319 and 290 days respectively. It should be remembered too that these quite unnecessary tragedies were all dealt with in a single hospital. If Birmingham may be taken as a random sample of the population the number of accidents due to electric fires would amount to something like 1,000 a year for the whole country, almost all of which could be prevented if the fires were compelled to carry a fixed light guard.

*Scalds.*—The prevention of scalds is a rather different problem. Something might be achieved by better design of kettles and other utensils, cooking stoves, &c., but the main defence must be by propaganda. We need a nation-wide campaign to bring this matter before the public: by radio, the Press, and cinema and perhaps most of all by personal contacts at Women's Institutes, Welfare and Maternity Centres and also in the schools for the older children.

Finally, there are two aspects of this problem which emphasize the urgent need to reduce the number of these accidents.

The first is the very considerable drain upon hospital services which the care of all these burns and scalds entails. Table VI shows that the 736 Birmingham cases (in one hospital)

TABLE VI.—OCCUPANCY OF HOSPITAL BEDS

|                             | Cases | Total days<br>in hospital |
|-----------------------------|-------|---------------------------|
| Industrial accident .. .. . | 232   | 8,697                     |
| Home accident .. .. .       | 504   | 19,602                    |
| Total                       | 736   | 28,299                    |

meant the occupancy of a hospital bed for no less than 28,299 days—and that figure would have been much higher if we had not had quite special facilities for treating these cases. All the burns treated in the hospitals of England and Wales must represent a total occupancy of well over a million bed-days each year, with all that means in services of doctors and nurses, engineers, clerks, cooks, laundry hands, &c.

My second point is this. Ten years ago a burn of 30% of the body surface was nearly always fatal—especially in a child. To-day that need not be so. Children with even 40 and 50% of the body burned can be saved by skilful treatment. But many of them will recover with grievously disfigured and sometimes disabled bodies—to endure unhappiness and to be a burden on the community throughout life. That surely is an additional reason why we should be preventing these unnecessary accidents.

**Dr. C. A. Boucher:** More than 8,000 persons are killed every year in England and Wales in the home and in everyday pursuits. If one limits the fatalities to those actually occurring in the home, then more than 6,000 fatal accidents occur annually. There has been no fall in this figure during the last ten years. On the contrary, in the under 5 age-group and in the over 65 age-group there has been an increase.

In 1945, the last year in which we have records, half of these fatalities occurred over the age of 65 years, while about one-fifth occurred in children less than 5 years old. The majority of the fatalities amongst the aged resulted from falls in the home.

One striking feature revealed by the figures for 1945 and the preceding years is the marked increase in deaths from suffocation mainly, as one would expect, in children under 1 year of age. These deaths resulted from soft pillows in the cot, overlying in the bed, and choking with solid food; this last factor has increased significantly over the period under review. There has also been an increase in deaths from coal-gas poisoning and from electricity.

What is the cause of these accidents in the home? The deaths show that 60% of the fatalities result from falls while 15% result from burns and scalds. It is not considered that structural defects in the home are primarily responsible for falls, burns and scalds; it is not believed that existing house design is the major cause. On the other hand, overcrowding in the home is a definite factor, especially in the case of accidents affecting children. Other causes are ignorance of the dangers existing in the home, carelessness and neglect about such dangers, and faulty appliances which look tempting and cheap in the shops and which can be purchased so easily by the non-discriminating person.

**Prevention.**—The Royal Society for the Prevention of Accidents has shown great energy and imagination in drawing the attention of the public to dangers in the home and this Society is the chief medium through which propaganda is initiated. An interdepartmental committee on accidents in the home was set up by the Home Secretary in 1947 to co-ordinate departmental action in connexion with the prevention of accidents in the home and to maintain contact with unofficial organizations interested in the subject. The Domestic Accidents Panel of the Building Requirements Sub-committee of the Ministry of Works and a Domestic Equipment Committee in the Ministry of Health are both giving attention to the safety aspect. From social surveys which take place every month enquiries are made about accidents which have occurred and the information collected is correlated. Some local authorities hold exhibitions about home safety, and the gas and electricity departments are assisting. The local education authorities are encouraging teachers to inform the children about home dangers and how they can be prevented. Short trailer films of about one minute are being shown at public cinemas, including one connected with burns and scalds, another connected with falls, while a longer film called "Playing with Fire" has been circulated by the Central Office of Information in their mobile units at meetings of Women's Institutes, &c., and on request at welfare clinics and other suitable places.

The Ministry of Health in a letter to women's magazines, women Press correspondents, the B.B.C., &c., have drawn the attention of the editors to the dangers of burns and scalds in the home. Pamphlets have also been prepared.

Personal education is of more value than impersonal propaganda. The education of the parents and other adults can take place in welfare clinics and through the medium of health visitors, district nurses and general practitioners. The education of the children, and this is very fruitful, should be through the teachers. With regard to the manufacturers of home appliances, one should aim to make the public critical of goods which they buy and, in time, public opinion will demand safe articles. On this aspect legislation might be an advantage.

**Mr. John Bunyan:** A system of first-aid treatment of injured hands has been tried and found satisfactory in some pits in the North of England. The arrangement is simple. A steel cabinet with a swing-down door is placed in convenient positions in the pit where hand accidents are most likely to occur. Every miner knows that on injuring his hand all he has to do is to lower the hinge lid of the cabinet where he will find a basin and bottles containing sodium hypochlorite and water which, on being emptied into the basin, provide the correct concentration of sodium hypochlorite. He immerses his injured hand and waits for the first-aid man who applies a simple silk envelope after ten minutes. The sodium hypochlorite removes the contaminated blood and blood clot and causes a clean blood clot to form, reduces traumatic inflammation and takes away pain. The envelope, which is simple to apply, gives complete protection to the wound and causes no pain on removal. Having thus protected the wound, it is not of such great moment that some hours may elapse before the patient can be adequately treated at hospital.

**Dr. Percy Stocks,** mentioning the work being done in America to reduce home accidents' thought that general appeals were unlikely to succeed and that each cause of accident would have to be attacked in detail. A necessary prelude to such action was to obtain good statistics and the General Register Office was doing three things to that end. Coroners' certificates were providing more detail than hitherto of the circumstances of fatal accidents and where they occurred. After lengthy discussion with experts over the water a classification both by nature of injury and cause of accident had been grafted into the International List, which was now designed for morbidity as well as mortality statistics. This contained definitions and enough detail of grouping to satisfy anyone. The teaching hospitals had in the past paid little attention to causes of accidents but now they were being asked to do so in the interests of prevention. It was hoped to secure sufficient information about in-patients during 1949 to provide some useful statistics in the full detail of the new list. This would mean hard work but he believed the hospitals could, in that way, make an important contribution to the eventual reduction of many kinds of accidents.

[December 6, 1948]

## DISCUSSION ON FOOD POISONING

**Dr. E. T. Conybeare:** *Administrative measures.*

Prominent among the administrative measures concerned with food poisoning in the past have been:

- (1) Encouragement by a Government department of two outstanding investigators of food poisoning.
- (2) Provision of a laboratory service for the special investigation of bacterial food poisoning.
- (3) The issue to medical officers of health of memoranda offering guidance in the investigation of food poisoning outbreaks and the provision of practical help to them in circumstances of exceptional difficulty attending such outbreaks.
- (4) The promotion of legislation facilitating the ascertainment of cases of food poisoning and useful in preventing it.

Before attempting to suggest possible lines of future development it may be as well to consider the lessons of the past.

In 1890, Ballard, after ten years' work in which, without any accurate bacteriology to help him, he clearly discerned the infective origin of most food poisoning and distinguished the toxin from the infection form of outbreak, wrote: "What does all this indicate as an efficient precaution against food poisoning? The grand precaution of all is the very commonplace one signified by the word *cleanliness* and it should be the business of the conservators of public health to see that this is observed as well as the business of every master or mistress of a family."

In 1925 Sir W. Savage, after over twenty years' study of the subject, postulated that if salmonella outbreaks could be controlled food poisoning would practically cease to exist as a public health problem. Savage thought that the key to this was first, a complete knowledge of the reservoirs of salmonella infection and then of the paths by which these bacilli

could reach human food; to help in this Savage wanted bacterial food poisoning made notifiable, and more attention paid to the investigation of clinically mild and numerically small outbreaks.

Fig. 1 is a chart of the actual numbers of outbreaks of food poisoning recorded as "reported" to the Ministry of Health between 1927 and 1947. Up to 1939 the source of

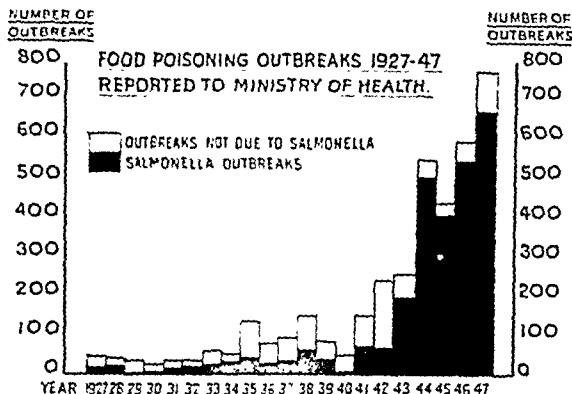


FIG. 1.

information was the Ministry's laboratory in London plus the special reports sent in by medical officers of health. After 1939 information was available through the regional laboratories of the Emergency Public Health Laboratory Service and its successor, the Public Health Laboratory Service. It is difficult to know the real meaning of the considerable increase in the number of reported outbreaks which started about 1942. Notification beginning in 1939 did not apparently produce any remarkable change. The war may have interfered. It is possible that from 1942 onwards when communal feeding became a more common practice and dried egg was used on a larger scale, there was a real increase in the number of outbreaks. Alternatively the apparent increase is only a result of the more frequent ascertainment of outbreaks resulting from the work of the Public Health Laboratory Service.

Past experience of administrative measures provides the following observations and suggestions:

**Memorandum.**—The current Ministry of Health memorandum on food poisoning is out of date. It was issued before food poisoning became notifiable and before the Public Health Laboratory Service came into existence and it does not mention staphylococcal enterotoxin. It should either be extensively revised or replaced by a new circular.

**Notification.**—Too much should not be expected of this procedure in connexion with food poisoning. Notification is bound to be an imperfect measure of incidence for a condition which, in its milder forms, escapes medical attention altogether and which, in any event, cannot be rigidly defined or recognized clinically with complete certainty. The main purpose of notification must still be to bring to the notice of the medical officer of health circumstances requiring further investigation or action of a kind which the general practitioner cannot be expected to undertake.

Hitherto the local data produced by notification, which was begun in 1939, have not been collected for central tabulation and analysis, but from January 1949, medical officers of health will be asked to include in their weekly return to the Registrar-General a note of the number of notified cases of food poisoning. These figures will be published as a total, and also by districts, in the Registrar-General's Weekly Return and, after correction for wrong diagnosis, the totals will be available in the Registrar-General's Quarterly Returns and, no doubt, will appear eventually in the Annual Statistical Review. It is likely that the data obtained in this way, apart from being more or less incomplete and therefore inaccurate as a measure of incidence, will be subject to fluctuations of an enigmatic kind comparable to those in the figures for the notification of dysentery to which Dr. J. Alison Glover has lately drawn attention. It would be a mistake to allow these data of notified cases to replace the collection of records of investigated outbreaks. The data obtained from notification should be combined with the information resulting from

the investigation of outbreaks so as to make possible a useful annual analysis by the Ministry of Health and the Ministry of Food.

*Laboratory Services.*—The regional laboratories of the Public Health Laboratory Service now cover practically every part of the country and are supported by central reference laboratories in which epidemiologically important procedures, like the typing of salmonellæ and staphylococci, can be done. It is now within the bounds of practical possibility for material from almost every notified case of food poisoning to be examined by competent bacteriologists.

It has been suggested that the routine laboratory investigation of food poisoning has become a waste of time. Although there are only a very small number of instances on record in this country in which, as a result of laboratory or other evidence obtained in the investigation of an outbreak of food poisoning, it has proved possible to take any effective preventive action, such as stopping the sale of infected food remaining unsold, the view that the routine laboratory investigation of food poisoning outbreaks is no longer worth while and that it ought to be entirely given up or limited in extent cannot be accepted. Present knowledge, at least in this country, is not sufficient to warrant this step.

Laboratory tests entirely divorced from epidemiological enquiries at the scene of an outbreak may be of little or no value. If they act too independently of one another neither the field epidemiologist nor the laboratory worker will ever solve such outstanding problems as are presented, for instance, by outbreaks in which, although food is a possible vector, it cannot be shown to contain a known bacterial pathogen or a chemical poison.

*Legislation.*—Ballard said nearly sixty years ago that the grand precaution of all was the commonplace one signified by the word cleanliness. To the extent that cleanliness of food depends on the cleanliness of persons it will not be easy to ensure it by legislation. It is, however, undoubtedly possible to legislate with some effect for environmental hygiene, i.e. for the cleanliness of places. The Food and Drugs Act 1938 contains special provisions in relation to premises used to prepare cooked meats for sale and to those used for the making of artificial creams, both of which are types of food liable to be concerned in food poisoning. The methods of food handling in catering establishments and other premises concerned in the sale and distribution of food rather than its preparation at present largely escape control by legislation. Here, as in food manufacture, the human link is the weakest in the chain.

There does not at the moment appear to be any special indication for further legislation relating, say, to catering establishments or to homes, which would be helpful in the prevention of food poisoning unless it be powers to prevent the employment in certain capacities related to food preparation or distribution of persons found to be healthy carriers of micro-organisms such as salmonellæ or staphylococci of potentially dangerous types. On this line of action, there is also the possibility of requiring all persons engaged in such occupations to undergo routine laboratory tests to acquit them of a potentially dangerous carrier state.

Greater or more specific legal powers than those available at present do not appear to be required in connexion with organizations which manufacture or distribute food on a large scale. Legal powers tend to be too slow in action to be of practical importance; their greatest usefulness seems to be that their existence is often sufficient to dissuade those who might be willing to risk both the public health and the heavy damages which their victims might obtain in a Court of Law.

In time it may be that health education and a more critical climate of public opinion, rather than legislation, will produce standards of food handling in catering establishments and in homes that will offer a maximum protection against bacterial food poisoning. Notwithstanding our present difficulties in meeting demands for the new building and the new equipment which these standards entail, it is not too early to begin to inform the public more fully in this matter, starting perhaps by drawing attention to the causes of food poisoning outbreaks which originate in the home.

Dr. V. D. Allison: Most important among the enterotoxin-producing bacteria as a cause of food poisoning are the coagulase-positive staphylococci. The enterotoxin is pre-formed in the infected food, so there must be suitable conditions as regards the type of food, its moisture content, the temperature to which it is exposed and an interval of time between the actual infection of the food and its consumption by the victims, a time during which the organisms multiply and produce toxin. The clinical syndrome is now well recognized—short incubation period (one to seven hours with an average of three hours), acute onset with abdominal pain, nausea, vomiting and often diarrhœa, the symptoms lasting from three to twenty-four hours followed by rapid recovery, even from a state of collapse. Enter-

toxin can be produced in the laboratory from food-poisoning strains of staphylococci by growing them for forty-eight hours in 0.2% nutrient agar in an atmosphere containing 30% CO<sub>2</sub>. Sterile filtrates from such cultures when taken orally by human volunteers in doses as small as 1–2 ml. give rise to the complete clinical picture of staphylococcal food poisoning.

The differentiation of serological types among coagulase-positive staphylococci, by Cowan (1939), Christie and Keogh (1940), and Hobbs (1948), and of bacteriophage types by Fisk (1942) and Wilson and Atkinson (1945), has been applied to field problems and has already added to our knowledge of the epidemiology of staphylococcal infections; the field is wide open for further investigation and progress. About 65% of coagulase-positive strains of staphylococci can be identified by phage typing and about 98% by serological typing—neither of the two methods is, as yet, practicable as a routine laboratory procedure.

The application of serological and phage typing to the investigation of outbreaks of staphylococcal food poisoning during the last three years has shown that the enterotoxin-producing strain may be isolated and identified from the suspected foodstuff in numbers ranging from 500,000 to more than 2,000 million organisms per gramme; it has also been isolated from the stools and vomit of victims and from the nose, nose and skin, or focus of skin sepsis in food-handlers who have manually handled the food, whether in the factory where there is large-scale production, in the restaurant or canteen where it is served, in the retail shop selling to individual customers, or in the home. These investigations prove beyond doubt that the main mode of infection of food by staphylococci is from the nose or hand of the food-handler to food which is manually handled, followed by storage of the food at temperatures which encourage multiplication of the organisms and production of enterotoxin. It can be readily appreciated that according to the stage at which infection of food occurs between preparation by the manufacturer and its ingestion by the victims, so the size of the outbreak will vary, from countrywide incidents down to canteen customers, shop clientele and family outbreaks.

During the last three years, I have phage-typed strains of staphylococci from 47 outbreaks of enterotoxin food poisoning. Strains from 26 of the outbreaks were isolated in this country from the incriminated foodstuff and frequently also from the nose or skin of a food-handler, and less often from the faeces and vomit of victims. The remaining 21 strains were received from Professor G. M. Dack, Chicago, Professor C. E. Dolman, Vancouver, Major A. R. Sandiford, Egypt, and Dr. E. S. Horgan, Khartoum. The foods from which the strains were isolated included beef, tongue, lamb, bacon, Vienna sausage, meat pie, glazed liver sausage, pork cheese, pressed beef, meat sandwiches, hake, potato salad, goat's milk, ice-cream, trifle and cheese. Bread, vegetables and fruit, fresh or cooked, have rarely been implicated as the vehicles of staphylococcal or indeed other food poisoning; in the case of bread and fruit this may be, in fact, due to the acid pH of the food. It is interesting to note that strains from 30 (64%) of the 47 outbreaks belonged to one phage and serological type designated "6/47, IIIc"; these included 13 strains received from the four sources abroad, the remaining 17 having been isolated in this country. Eight of the strains belonged to phage type "42D", including three from Chicago, one from Egypt and four from this country. In passing it may be noted that phage type "42D" is the strain commonly found in raw cow's milk and identified by Williams Smith as a frequent cause of bovine mastitis—one of the strains from Egypt was isolated from cheese which seems to be a not uncommon vehicle of staphylococcal food poisoning in that country as all four strains received from this country were isolated from cheese. On the other hand a strain isolated from a mixture of milk from cow, goat, sheep and camel which caused an outbreak in the Sudan was traced to the goat's milk and identified as phage type "6/47". Of the remaining nine strains in the series three could not be typed and six were divided among three other phage types. When it is realized that by the use of 22 phages it is possible to identify between 20 and 30 phage types and subtypes of coagulase-positive staphylococci, it would seem to be significant that strains from 81% of 47 outbreaks belong to only two phage types.

I would not for one moment suggest that all staphylococci of phage type "6/47" are enterotoxin producers, as this type appears to be one of the commonest types found in the nose of man, but another phage type, designated "3A", is at least as common in the nose and has not yet been found as a cause of staphylococcal food poisoning although it is outstanding as a cause of pemphigus neonatorum.

On occasions reheated foods have been implicated as the cause of enterotoxin food poisoning and it is, of course, known that staphylococcal enterotoxin resists boiling for at least thirty minutes. The staphylococci are killed by the heat treatment but the enterotoxin remains active and potent, and in such cases bacteriological examination by the laboratory of specimens of suspected food and faeces and vomit from victims will yield negative results. The difficulties in attempting to trace an outbreak of this type to its source can readily be appreciated. The mere finding of one or more nasal or skin carriers among the personnel



handling the suspect foodstuff is not alone sufficient grounds for implicating them as the source of the outbreak or suspending them from duty. But if, in the absence of cultures of staphylococci from victims or suspected food, we find that a food-handler is harbouring in his nose, or on his hands, a strain of staphylococcus belonging to a phage type (6/47) pre-eminent as an enterotoxin producer and cause of food poisoning, we are on surer ground in recommending his suspension from food-handling duties until he ceases to be a carrier.

Even in outbreaks in which the same phage or serological type of staphylococcus has been isolated from the stools of victims, from the suspect foodstuff and from the nose or hands of a handler of the food, there is another aspect to be considered. My colleagues, Dr. Mair E. M. Thomas and Dr. Joan Edwards at Colindale, have found that coagulase-positive staphylococci are present in the stools of approximately 33% of routine specimens sent to the laboratory, in the absence of any suggestion of staphylococcal infection of the gut or of food poisoning. In a series of paired strains of typable coagulase-positive staphylococci, isolated from the nose and stools of 31 individuals, the strains from 21 pairs were the same. In the remaining 10, strains from stool and throat were the same type in four instances; in six instances the strain from the stool belonged to a type different from that found in the nose, the throat either not having been swabbed or found negative. The conclusion I draw from this is, that the sources of coagulase-positive staphylococci isolated from the stool of an individual are either the nose, in a person who is a nasal carrier, or the food consumed by the individual or both. Which of us does not daily ingest in our food hundreds, perhaps thousands, of staphylococci derived from human hands and nose without ill-effect? It is perhaps not surprising therefore that they should appear in the stool. Such findings must make us cautious in interpreting as staphylococcal food poisoning results based solely on finding the same type of staphylococcus in a foodstuff, in the stool of a person who has partaken of it, and in the nose or on the hands of someone who has handled it. We must have, in addition, the typical clinical and epidemiological picture, and if possible a count of the number of viable staphylococci per gramme in the suspect food. I have recently had specimens from an outbreak of suspected staphylococcal food poisoning in which the same phage type of staphylococcus was isolated from the stools of victims and from the *unheated* suspect food—but counts in the latter were less than 100 per gramme. I would be very loth to accept such tenuous evidence as proof of staphylococcal food poisoning. If I were asked what would be the minimum number of viable coagulase-positive staphylococci per gramme of food I would accept as supporting evidence of staphylococcal food poisoning, I would feel diffident in giving a figure. Tentatively, I might suggest about 500,000 per gramme, but even that might be too high if the organism were a potent enterotoxin-producer.

In the majority of outbreaks of staphylococcal food poisoning the evidence against the staphylococcus is largely circumstantial, as in only a few instances is it possible or practicable to determine that the suspect strain is capable of producing enterotoxin, by the only methods at present at our disposal—the human volunteer or feeding to monkeys. The human volunteer is rarely available, and monkeys when available are capricious in their sensitivity and reaction to oral administration of staphylococcal enterotoxin. The kitten test for staphylococcal enterotoxin is no longer accepted, and there is a great need for a bench test. Attempts to devise such a test have so far only shown the many difficulties that have to be overcome to make it specific for enterotoxin.

The human nose is the commonest reservoir of coagulase-positive staphylococci, but investigations by my colleague Dr. Betty Hobbs show that the skin may be an important secondary reservoir in the absence of carriage in the nose and that the clean-looking, healthy, healing cut may be teeming with staphylococci, just as Colebrook and Ross (1947) obtained a profuse culture of group A streptococci which caused infection in a patient from the scab on the almost healed abrasion on a surgeon's elbow.

The basis of preventive measures is *clean* food, prepared by *clean* persons, using *clean* utensils in *clean* kitchens, with avoidance of manual handling of food after cooking or processing, and preservation of food in the refrigerator (Allison, *et al.*, 1949).

#### REFERENCES

- ALLISON, V. D., HOBBS, B. C., and MARTIN, P. H. (1949) *Monthly Bull. Min. Hlth. Pub. Hlth. Lab. Serv.*, 8, 38.  
CHRISTIE, R., and KEOGH, E. V. (1940) *J. Path. Bact.*, 51, 189.  
COLEBROOK, L., and ROSS, W. P. D. (1947) *Lancet* (ii), 792.  
COWAN, S. T. (1939) *J. Path. Bact.*, 48, 169.  
FISK, R. T. (1942) *J. infect. Dis.*, 71, 153, 161.  
HOBBS, B. C. (1948) *J. Hyg.*, 46, 222.  
WILSON, G. S., and ATKINSON, J. D. (1945) *Lancet* (i), 647.

Dr. Joan Taylor: In recent years the number of proven salmonella infections has increased (Table I), but it is impossible to say whether this change in incidence is real or is the result of improved laboratory facilities.

TABLE I.—HUMAN SALMONELLOSIS IN ENGLAND AND WALES\*

|                              |    | 1923-39 | 1940-41 | 1942-43 | 1944-45 | 1946-47 |
|------------------------------|----|---------|---------|---------|---------|---------|
| <i>Salm. typhi murium</i>    | .. | 235     | 112     | 144     | 505     | 1,046   |
| .. <i>enteritidis</i>        | .. | 54      | 28      | 35      | 90      | 63      |
| .. <i>thompson</i>           | .. | 49      | 50      | 28      | 39      | 66      |
| .. <i>newport</i>            | .. | 29      | 19      | 21      | 108     | 39      |
| .. <i>cholerae suis</i>      | .. | 14      | 3       | 4       | 2       | 3       |
| .. <i>bovis morbillicans</i> | .. | 8       | 3       | 9       | 9       | 11      |
| .. <i>dublin</i>             | .. | 8       | 6       | 4       | 4       | 31      |
| Other types                  | .. | 32      | 25      | 5       | 9       | 19      |
| <i>Salm. anatum</i>          | .. | —       | 2       | 6       | 13      | 8       |
| .. <i>montevideo</i>         | .. | —       | 2       | 18      | 42      | 29      |
| .. <i>oranienburg</i>        | .. | —       | —       | 41      | 50      | 27      |
| .. <i>meleagridis</i>        | .. | —       | —       | 8       | 16      | 3       |
| .. <i>tennessee</i>          | .. | —       | —       | 4       | 6       | 6       |
| Other types                  | .. | —       | 19      | 41      | 68      | 86      |
| Total                        |    | 429     | 269     | 368     | 961     | 1,437   |

\*The figures for the years 1923 to 1939 were compiled from the Annual Reports of the Chief Medical Officer of the Ministry of Health; those for subsequent years from the weekly returns to the Public Health Laboratory Service, together with those from the Salmonella Reference Laboratory.

*Salmonella infections.*—It is obvious that the types which were commonly found in this country prior to 1940 still occur more frequently than do other types. The most frequent cause of salmonella food-poisoning is *Salmonella typhi murium* followed by *Salmonella enteritidis*, *Salmonella thompson* and *Salmonella newport*. A line has been drawn across the chart dividing the types occurring pre-war from those occurring during subsequent years. The types below the line were new to this country, their appearance in human infections coinciding with the distribution of dried egg to the general public. An investigation of salmonella types occurring in dried egg (M.R.C. Special Report Series, No. 260) undertaken by the Public Health Laboratory Service showed that these new types were present in this food. Of the new types isolated, the five most commonly found in dried egg were those which accounted for the majority of the new types in human infection.

*Animal hosts.*—It has been said that animal reservoirs are the most important factor in human salmonellosis. Mice and rats are known to be carriers of *Salmonella typhi murium* and *Salmonella enteritidis* and a number of outbreaks of food poisoning have been traced to this source. Outbreaks of *Salmonella dublin* infection, a disease of bovines, have not uncommonly been traced to milk, but a recent survey of this infection in bovines (Field, 1948) has shown that though this disease is relatively common in Mid and West Wales, infection having been proved on 66 farms, no cases of human infection were reported during the period of the survey. Nevertheless, an outbreak of *Salmonella dublin* infection in Aberdeen (Henderson *et al.*, 1948) was traced to milk. For infected milk to give rise to cases of human disease it is obvious that certain conditions such as temperature, humidity and time interval suitable for the multiplication of organisms are necessary, so that an infective dose is ingested by the patient. Poultry are not uncommonly infected with salmonella organisms. Excluding *Salmonella pullorum* and *Salmonella gallinarum*, *Salmonella typhi murium* and *Salmonella thompson* have been responsible for the majority of outbreaks of disease among chicks in recent years (Gordon and Buxton, 1946), nevertheless no cases of human infection due to these organisms were connected with this source. In contrast with this, cases of human infection due to *Salmonella enteritidis* and *Salmonella typhi murium* have been traced to the eating of infected duck eggs. In these birds the ovary becomes infected giving rise to infection of the egg contents. In the hen the ovary is almost never affected. The hen egg occasionally may be infected by the passage of organisms through the shell as the result of faecal contamination. The importance of cats and dogs as a reservoir of salmonella infections is not yet known, but recently a case of *Salmonella typhi murium* infection in a child was traced to a pet cat, and *Salmonella thompson* was isolated from a dog with diarrhoea though no human cases occurred.

A source of infection, sometimes overlooked, is the use of so-called rat and mouse "virus" preparations for the destruction of vermin. Recently, from a virus preparation used in a public restaurant were isolated the human and danyasz varieties of *Salmonella enteritidis*.

It is illogical that efforts are made to stop the handling of food by human excretors of the salmonella group yet living cultures of these organisms may be used deliberately in kitchens. One outbreak (Dathan *et al.*, 1947) was traced to this source.

The rôle of the human carrier is not known as it is often difficult to decide whether a particular case is the cause or the result of the eating of infected food. After salmonella infections patients commonly excrete the infecting organism for four to six weeks and some remain carriers for months. The dose of organisms necessary to cause human disease is large; Hormaechi *et al.* (1936) found that 2,000 – 4,000 million organisms of *Salmonella typhi murium* sometimes caused mild diarrhoea in human volunteers.

*Dysentery*.—Organisms of this group may cause an explosive outbreak of food poisoning, such as that which occurred at Holborn (Scott, 1934). About 20 persons were infected with *Sh. sonnei* after partaking of pease-pudding, the latter having been infected by a child convalescing from the disease.

*Paracolon organisms*.—The importance of this group of organisms as the cause of food poisoning is not yet known. They are a group, difficult to define, with some of the characteristics of the salmonella and the *Bact. coli* groups. Last year an outbreak of gastro-enteritis occurring among school children was investigated. From the faeces of cases was isolated a single serological type of paracolon bacillus. From another outbreak of food poisoning occurring in a P.O.W. camp in the Midlands was isolated the same serological type. In addition, this organism has been isolated from two sporadic cases of gastro-enteritis. Dr. Hobbs fed cultures to two human volunteers both of whom had symptoms similar to those of the other cases, thereby proving that the organism was the cause of the disease.

More research will be necessary to assess the importance of other members of the paracolon group as a cause of food poisoning.

In conclusion it must be emphasized that food poisoning caused by the organisms discussed is dependent on the assimilation of a relatively large dose, which in turn is dependent on the food, temperature, moisture and time interval being suitable for the multiplication of these organisms.

An appreciation of these factors and the education of food-handlers should lead to a fall in the incidence of food poisoning.

#### REFERENCES

- DATHAN, J. G., MCCALL, A. J., ORR-EWING, JEAN, and TAYLOR, JOAN (1947) *Lancet* (ii), 711.  
FIELD, H. I. (1948) *Vet. J.*, 104, 251.  
GORDON, R. F., and BUXTON, A. (1946) *Vet. J.*, 102, 187.  
HENDERSON, A., MICKIE, E. J., RAE, H. J., and SMITH, J. (1948) *Scottish Hlth. Bull.*, 41, 28.  
HORMAECHI, E. (1947) *Spec. Rep. Ser. med. Res. Coun., London*, No. 260.  
HORMAECHI, E., PALUFFO, C. A., and ALEPPO, P. L. (1936) *Arch. urg. Med.*, 9, 113.  
SCOTT, H. HAROLD (1934) *Some Notable Epidemics*. London.

## Section of Surgery

President—JULIAN TAYLOR, C.B.E., M.S., F.R.C.S.

[December 1, 1948]

### DISCUSSION ON HIRSCHSPRUNG'S DISEASE

Mr. T. Twistington Higgins: *Congenital idiopathic dilatation of the colon, or Hirschsprung's Disease*, belongs to the group of *neuromuscular inco-ordinations*—a group which has a sinister significance for the young, including, as it does, pyloric stenosis in infants and achalasia of the œsophagus. It also includes many lesions in the *urinary tract* and some in the *biliary tract*.

*Cyst of the common bile duct* is a rare disorder, occasionally occurring in children. In the three instances I have had to deal with, it was a striking fact that, after evacuation of the cyst, a sound passed into the duodenum with ease. There was apparently no mechanical obstruction. It would seem that this condition, therefore, falls into the same group, at least in some instances.

These neuromuscular inco-ordinations are always local and single manifestations. It is often stated that the Hirschsprung colon is accompanied by analogous dilatation in the urinary tract but this has not been our experience.

Some local cause is usually the determining factor and since the pathogenesis is obscure, it is not surprising to find that treatment is varied and results uncertain.

*Total colectomy*.—This early operation did not relieve the obstruction as the small intestine dilated to a size comparable with the original colon.

*Conservative treatment* was formerly advocated by Hurst, e.g. digital or mechanical dilatation of the lower bowel, aperients, abdominal massage, &c.

*Sympathectomy*.—Then came the era of sympathectomy, increasing in extent, as knowledge

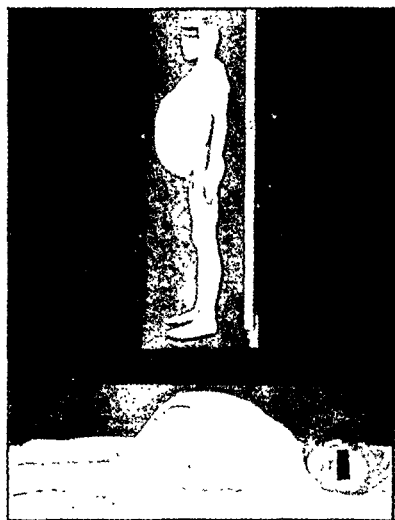


FIG. 1.—Photograph of a boy of 15 years. Repeated spinal anæsthetics and sympathectomy had given no relief. Later cured by excision of the recto-sigmoid. Lower photograph shows peristalsis.

of the sympathetic anatomy broadened. In *obstinate cases* partial colectomy of "redundant loops" was combined. With these procedures the name of my colleague, Barrington-Ward, must be honourably associated.

*Spinal anæsthesia*.—My old "chief", Telford of Manchester, showed us that a simple spinal anæsthetic could achieve as much as sympathectomy, *provided the anterior roots* were paralysed at least as high as T.5. Margaret Hawksley emphasized that repeated administrations might be necessary, and that some time might elapse before the final result could be assessed.

It is illogical that efforts are made to stop the handling of food by human excretors of the salmonella group yet living cultures of these organisms may be used deliberately in kitchens. One outbreak (Dathan *et al.*, 1947) was traced to this source.

The rôle of the human carrier is not known as it is often difficult to decide whether a particular case is the cause or the result of the eating of infected food. After salmonella infections patients commonly excrete the infecting organism for four to six weeks and some remain carriers for months. The dose of organisms necessary to cause human disease is large; Hormaechi *et al.* (1936) found that 2,000 – 4,000 million organisms of *Salmonella typhi murium* sometimes caused mild diarrhoea in human volunteers.

*Dysentery*.—Organisms of this group may cause an explosive outbreak of food poisoning, such as that which occurred at Holborn (Scott, 1934). About 20 persons were infected with *Sh. sonnei* after partaking of pease-pudding, the latter having been infected by a child convalescing from the disease.

*Paracolon organisms*.—The importance of this group of organisms as the cause of food poisoning is not yet known. They are a group, difficult to define, with some of the characteristics of the salmonella and the *Bact. coli* groups. Last year an outbreak of gastro-enteritis occurring among school children was investigated. From the faeces of cases was isolated a single serological type of paracolon bacillus. From another outbreak of food poisoning occurring in a P.O.W. camp in the Midlands was isolated the same serological type. In addition, this organism has been isolated from two sporadic cases of gastro-enteritis. Dr. Hobbs fed cultures to two human volunteers both of whom had symptoms similar to those of the other cases, thereby proving that the organism was the cause of the disease.

More research will be necessary to assess the importance of other members of the paracolon group as a cause of food poisoning.

In conclusion it must be emphasized that food poisoning caused by the organisms discussed is dependent on the assimilation of a relatively large dose, which in turn is dependent on the food, temperature, moisture and time interval being suitable for the multiplication of these organisms.

An appreciation of these factors and the education of food-handlers should lead to a fall in the incidence of food poisoning.

#### REFERENCES

- DATHAN, J. G., MCCALL, A. J., ORR-EWING, JEAN, and TAYLOR, JOAN (1947) *Lancet* (i), 711.  
FIELD, H. I. (1948) *Vet. J.*, 104, 251.  
GORDON, R. F., and BUXTON, A. (1946) *Vet. J.*, 102, 187.  
HENDERSON, A., MICKIE, E. J., RAE, H. J., and SMITH, J. (1948) *Scottish Hlth. Bull.*, 41, 28.  
HORMAECHI, E. (1947) *Spec. Rep. Ser. med. Res. Coun., London*, No. 260.  
HORMAECHI, E., PELUFFO, C. A., and ALEPPO, P. L. (1936) *Arch. urg. Med.*, 9, 113.  
SCOTT, H. HAROLD (1934) *Some Notable Epidemics*. London.

and encounter faeces, then it can be assumed that the distal segment is short, which would seem a good prognostic sign.

*Radiologically.*—Variations in the length and calibre of the distal segment can be demonstrated, and to some extent the effects of treatment can be assessed.

#### SUMMARY

There are three types of megacolon:

(1) *Acquired* ("Pseudo-Hirschsprung").—The aetiology is distinctive, the treatment is usually comparatively simple, and the prognosis good.

(2) *True Hirschsprung—mild type.*—The distal segment is relatively short and wide. Simple treatment by spinal anaesthetics and so on may give relief, and the prognosis is relatively good.

(3) *True Hirschsprung—severe type.*—In this group, the distal segment is long and narrow. The clinical picture is intractable and relentless from birth. Treatment by spinal anaesthesia, sympathectomy and so on does not afford effective relief.

It is in this group, in particular, that our treatment must be improved if young lives are to be saved, and much misery curtailed.

We may hope that some day a better understanding of the autonomic nervous system will enable us to control its vagaries in the young by non-surgical methods, but at present such an understanding is denied us. The only alternative seems to lie in surgery.

Mr. F. Douglas Stephens: In a previous paper read to the Proctological Section in July 1948 (*Proceedings*, 41, 831) I made the clinical distinction between two groups of cases exhibiting a dilatation of a varying length of large intestine without any obvious organic obstruction to account for it.

These two groups have characteristic clinical patterns and radiological appearances and include Group I, or Hirschsprung's Disease, and Group II, or Idiopathic Megacolon. In the previous paper the latter group was referred to as "Chronic Constipation".

I outlined the clinical characteristics and the radiological findings, and briefly discussed the course and treatment so far administered in these series of cases. The characteristic radiological findings of Groups I and II, as assessed by Dr. B. C. H. Ward, are illustrated in fig. 1. Tubular dilatation is the term adopted now to replace "long wide distended loop" in the previous paper.

Hirschsprung's disease      Terminal reservoir      Tubular dilatation

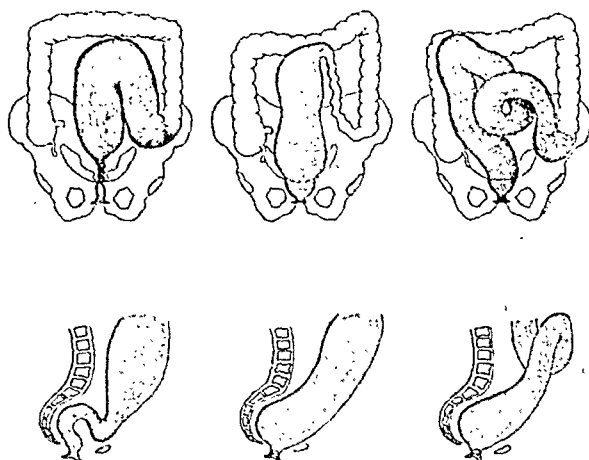


Fig. 1.—Radiographic appearances. (From *Lancet*, 1949 (1), 8—by permission)

In Group I the treatment, both medical and surgical, has been unsuccessful, and cases were produced at this previous meeting to demonstrate these features. Two-thirds of the cases in this group have suffered acute attacks of intestinal obstruction under one year of age.

In Group II the children are relatively fit, the condition seems to run a benign course, responding to medical measures with relapses from time to time. A large number have been cured by repeated regular bowel washouts over a period of several weeks or months.

Eight of these cases had an operation of one form or another on the sympathetic nervous

*Antispasmodic drugs.*—Finally, there appear in the literature from time to time reports of small groups of cases, treated by antispasmodic drugs of increasingly complex names and formulæ (Mecholyl Bromide and Syntropan).

Now all these various lines of treatment can claim their successes but all have to admit disappointments and frank failures.

Moreover, the record of these older children does not represent the complete story. There is no doubt that genuine Hirschsprung's disease carries a very high mortality rate, particularly in early life. Barrington-Ward, in a review of 30 cases, found that no fewer than 20 were dead before the age of 3 years, so that the children we see in later years are, in reality, the survivors.

It is clear that in Hirschsprung's disease there are marked differences in degree, differences which are in fact so striking as almost to suggest that we are dealing with different diseases. We would do well to address ourselves particularly to this point—to review our present investigational methods and diagnostic standards. Obviously, if we can say: "This is a mild case and will respond to simple measures", or "This is severe, and certainly will not do so", we shall clarify our ideas as to treatment. It is, of course, treatment of the severe cases which must exercise us most.

*Ætiology and Pathology.*—The only striking fact about the *ætiology* is the preponderance in boys. M : F—5 or 6 : 1. There appears to be a remarkable analogy to pyloric stenosis and the various urinary tract lesions. It would seem that the male sex has yet another heavy burden to bear.

*Pathology:* The known facts are simple enough. They are those of an obstruction without any obvious mechanical cause. The *proximal bowel* shows hypertrophy of the propulsive muscle with gross dilatation, and secondary inflammatory changes of various degrees. In the distal segment there is narrowing and apparent loss of function. The level at which this change occurs is variable, but the common site is in the pelvi-rectal region. But it may be lower or, more rarely, higher.

In the past, attention has tended to focus upon the huge proximal colon, but we now know that its removal, even total colectomy, does not remove the obstruction. The new proximal gut undergoes identical dilatation. It seems clear that the crux of the matter must lie in the distal segment A to B (fig. 3).

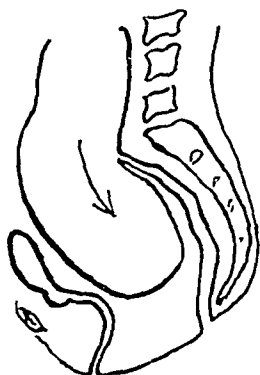


FIG. 2.—Diagram to show mechanism of acute obstruction in infancy. The proximal loop becomes progressively distended. Impaction in the pelvis determines complete obstruction. The condition can be relieved by the passage of a rectal tube and gradual decompression.

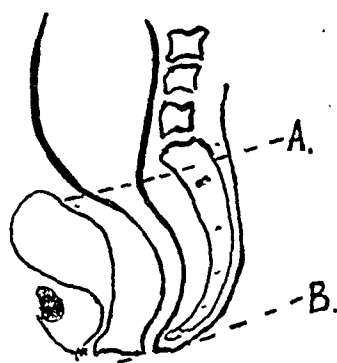


FIG. 3.—Diagram to show proximal and distal segments.

*Clinically.*—We can endeavour to distinguish any variations in this rectal segment and see whether these can be correlated with variations in the type or severity of the disease, thus giving us a clue to prognosis and treatment.

In the first place we have to sort out those cases of *acquired megacolon*, quite a different entity. Here, some anal lesion—congenital narrowing or chronic painful fissure—induces persistent constipation which may be sufficiently severe to lead to gross dilatation of the colon. Indeed, the barium picture may closely simulate true Hirschsprung. A rectal examination will usually reveal the anal abnormality and the rectum will almost certainly be found loaded with feces. In true Hirschsprung's disease, the anal canal appears perfectly normal and the rectum is empty. If the examining finger should enter the dilated proximal bowel

In these 11 cases the bowels now act regularly without abdominal distension or incontinence. The motions are still ribbon-like in shape, denoting that a small pathological anal segment still remains. There has been no mortality in this series of operations. In 5 cases complications of varying severity have occurred. 3 have had post-operative retention of urine which quickly subsided, except in one case which is only now improving after one month. Alterations in the technique of dissecting the rectum from the fascia propria, instead of removing the fascia with the rectum, may possibly account for the absence of this complication in the last few cases. One child had a mild form of narrowing at the anastomotic site which was easily dilated *per rectum* with the finger.

One child had a minor degree of faecal incontinence, but he is responding satisfactorily to training.

#### REFERENCES

- STEPHENS, F. D. (1948) *Proc. R. Soc. M.*, **41**, 831.  
 SWENSON, O., and BILL, A. H., Junr. (1948) *Surgery*, **24**, 212.  
 — (1948) Personal Communication.

**Dr. Martin Bodian:** *Pathology.*<sup>1</sup>—Failure to elucidate the aetiology of Hirschsprung's disease has been conditioned by two main misconceptions:

- (1) That all cases of idiopathic megacolon are cases of Hirschsprung's disease; and
- (2) that the dilated bowel is the site of the primary pathology.

The histo-pathological examinations in these investigations were confined to cases with radiologically and/or pathologically demonstrable narrow or normal terminal segment of bowel. The primary pathology could invariably be traced to this terminal segment and the dilated bowel was considered to be the site of secondary pathology.

The pathological material at the time of the report to the Section, Dec. 1, 1948, consisted of 15 specimens. The first 2 were derived from post mortems, performed in 1947: One on an infant of 15 days old presenting with acute intestinal obstruction. Terminal ileum, caecum, ascending and transverse colon were moderately dilated, but the distal colon from the splenic flexure downwards and the rectum were of normal diameter. 14 specimens came from children with chronic Hirschsprung's disease, of ages varying from 18 months to 13 years. One of these was a post-mortem case, 12 were surgical specimens after recto-sigmoidectomy, that is removal of the narrow terminal segment of bowel, and one specimen was an excised sigmoid colostomy loop.

Blocks were examined from consecutive levels of the entire intestinal tract in the two post-mortem cases and of the complete surgical specimens. The pathological findings, demonstrated in both intramural plexuses of Auerbach and Meissner, were uniform in all 15 specimens: complete absence of parasympathetic ganglion cells was noted throughout the entire narrow segments which varied from 5–18 cm. in length. Moreover, this aganglionic segment extended beyond the narrow bowel into the hypertrophied and dilated part for a distance of 1–5 cm. Proximal to the pathological segments, ganglion cells were always perfectly normal, though somewhat scantier in a short transitional zone. No inflammatory changes of significance were noted in the intramural plexuses of any of the specimens, and the pathological features were not considered to have resulted from inflammation. A degenerative lesion cannot be definitely excluded on histological grounds alone, but circumstantial clinical evidence is strongly in favour of a congenital lesion, and the histology is compatible with an agenesis of ganglion cells.

The pathological segments always extended right down to the anus, and included rectum, or, in addition, a varying part of sigmoid colon. The longest segment observed in the group came from the previously mentioned infant, in whom no ganglion cells were found distal to the splenic flexure.

All these findings were assessed against the background of a comparable control series, which consisted of 11 specimens of sigmoid colon, rectum and anus. Numerous ganglion cells were found at close spacing throughout the entire segments down to a few mm. from the anocutaneous junction.

Since this report to the Royal Society of Medicine, 5 more cases of Hirschsprung's disease have had rectosigmoidectomy performed, and the pathological investigations in all these cases yielded the same results as above. The total number in the series so far is, therefore, 20.

#### CONCLUSIONS

- (1) Hirschsprung's disease can be defined against idiopathic megacolon by its characteristic clinical picture, and the radiological pattern of a narrow distal segment of bowel.
- (2) Neurohistological investigation of a consecutive series of 20 cases of Hirschsprung's

<sup>1</sup>See BODIAN, M., STEPHENS, F. DOUGLAS, and WARD, B. C. H. (1949) *Lancet* (i), 6.



system, and six of these were diagnosed as Hirschsprung's disease, one as ? Hirschsprung's disease and one as megacolon. The results of these operations are very encouraging, but, in view of the fact that they would all have had thorough bowel preparation prior to operation, I am not certain now what part the operation played in the alleviation of the symptoms.

No cases in Group II have died.

I wish to acknowledge the work of my American colleagues, Swenson and Bill, whose article on this subject appeared in *Surgery* of August 1948, and whose work I saw personally one year ago during my short visit to the Boston Hospital for Children. They point out that there is this group in which a narrow spasmodic segment can be demonstrated radiographically below the dilated bowel if it is carefully looked for. They also concluded on clinical grounds that this segment was the obstructing factor, and instanced the case of relapse following closure of the sigmoid colostomy. They therefore removed the segment distal to the colostomy, joining the proximal bowel to the anus by the pull-through technique with preservation of the sphincter. They have now successfully treated many cases in this way (Swenson, 1948).

The treatment given to 12 children in Group I in this series embodies the principles suggested by Swenson, but varies in some points in technique.

A *staged rectosigmoidectomy* is performed by the pull-through technique, with preservation of the anal sphincter.

*Stage 1.*—After a preliminary course of bowel washouts, a right-sided transverse spur colostomy is made to defunction the distal colon.

*Stage 2* is the rectosigmoidectomy using an abdominoperineal approach.

There are some differences in this technique from that adopted in cancer surgery:

(a) The narrow segment is delineated and this portion of intestine is finally excised, together with half the funnel-shaped transition segment between the dilated and narrow portions (fig. 2).

(b) The rectum is dissected from its supporting fascia propria distally as far as the levator



FIG. 2.—The dilated sigmoid colon is seen narrowing down in the region of the rectosigmoid.

ani muscles, as opposed to the total removal of the perirectal tissues for malignant conditions.

(c) The narrow segment is then totally intussuscepted out of the pelvis through the anus, and this differs from the technique of Swenson, who divides the intestine within the abdomen before pulling it through the everted anus. The prolapsed segment is then excised, leaving about  $\frac{1}{2}$  in. of everted anal canal to which the hypertrophied colon is anastomosed. The pelvic floor is then reconstituted.

*Stages 3 and 4* are crushing of the spur and closure of the colostomy.

Here is a summary of the *short-term results*.

Of the 12 cases which have had the rectosigmoidectomy procedure, 11 are now completed, and 1 awaits closure of the colostomy. The post-operative period varies between three months and one week.

Mr. Denis Browne: The following six figures illustrate the method, devised by me of intussuscepting the narrow segment of bowel through the anus, and resecting the resulting prolapse. This technique was used in most of the cases described by Mr. Stéphen.

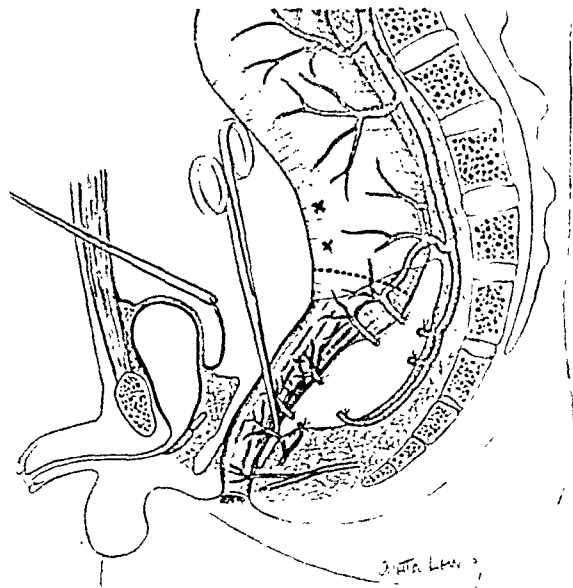


FIG. 1.

FIG. 1.—Diagram of the anatomy showing the freeing of the narrowed rectosigmoid and the ligation of its arterial supply.

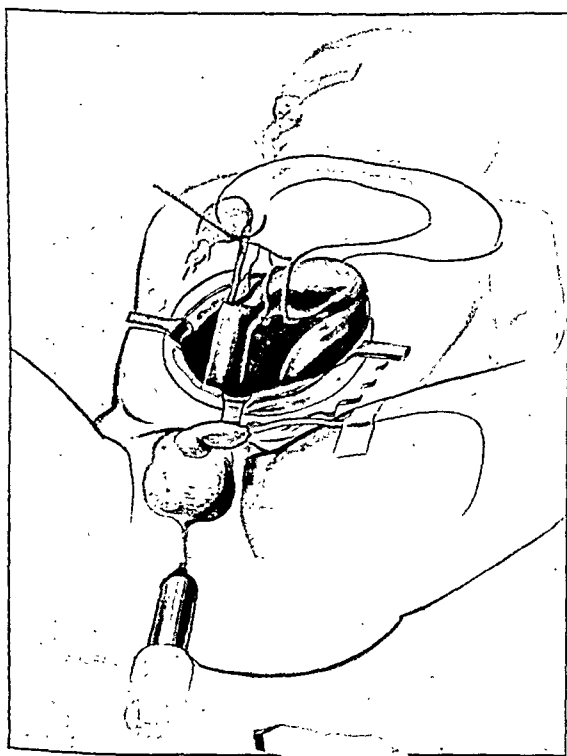


FIG. 2.

FIG. 2.—Showing the passage of a sigmoidoscope through the anus into the freed bowel which is to be resected. Two needles, 18 in. in length, are passed through the bowel into the sigmoidoscope at a point carefully selected as the centre of the section to be resected. They carry long loops of strong braided silk.

FIG. 3.—Enlarged diagram of the passage of the needles into the sigmoidoscope.

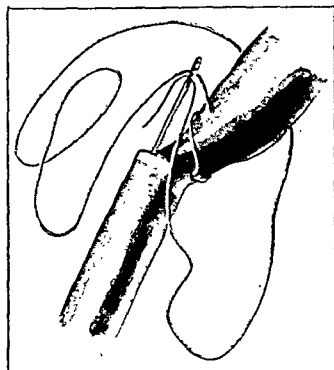


FIG. 3.

disease revealed absence of parasympathetic ganglion cells from the intramural plexuses of the narrow intestine and a small adjoining segment of dilated colon.

(3) This suggests a uniform pathology in Hirschsprung's disease, accounting for the lack of co-ordinated propulsive movement of the distal segment of bowel.

(4) This distal colonic obstruction leads to secondary dilatation and hypertrophy in the bowel proximal to it.

(5) Surgical removal of the pathological distal segment would thus appear to be a rational therapeutic approach to the problem of Hirschsprung's disease.

Dr. Richard Meyer: During the past eleven years 60 children have been admitted to the Birmingham Children's Hospital because of severe chronic constipation and the diagnosis of Hirschsprung's disease has had to be seriously considered in all these children. We have, however, found only 7 proved cases of megacolon in this series—about a quarter as many as at Great Ormond Street. Dr. Comay and I have studied these cases.

The differential diagnosis is of interest. Among the 60 children we found one case of hypothyroidism and another of steatorrhœa, both of which presented as cases of constipation with large abdomen and who narrowly escaped the surgical treatment then in vogue. There were 4 cases of anal stenosis and 7 children with constipation of clearly psychogenic origin. It is noteworthy that 2 cases of megacolon had been operated on for pyloric stenosis before their admission.

The bedside diagnosis of Hirschsprung's disease is difficult. There is no pathognomonic symptom or sign. We have found a history of constipation from birth, wasting, abdominal enlargement, visible peristalsis and fecal incontinence present or absent in both megacolon and other types of constipation.

There are, however, two bedside tests which help:

(1) The great majority of young children tolerate a rectal examination so placidly that, provided an anal fissure is not present, marked resentment of the examination suggests that the constipation is of psychogenic origin.

(2) If a simple soap and water enema is ejected straight away we think that this virtually excludes Hirschsprung's disease.

As far as X-ray diagnosis is concerned we ignore the length of colon as shown in the X-ray. Robbins has shown in an analysis of post-mortem material that there is no correlation between colonic length and previous bowel habit. The word *dolichocolon* is not a diagnosis and should not be used as such. The width of the colon is deceptive except in advanced cases of megacolon.

X-ray pictures taken immediately after evacuation of a barium enema are untrustworthy because naughty children may only evacuate a token amount, though by next day their colon is usually quite empty. We think that pictures taken twenty-four and forty-eight hours after a barium enema has been given show a truer picture of the colon's activity than do single films. The case with simple constipation has piled up the barium into his rectum at the end of forty-eight hours. A case of Hirschsprung's disease, in our limited experience, still retains barium in his colon at this time. Cases of the reservoir type of constipation may retain barium throughout a contracted and well-hausted colon at the end of forty-eight hours. We have found these cases very difficult to treat and think that they suffer from something more than a simple rectal constipation. Twenty-four and forty-eight hours' follow-up X-ray pictures should always be taken before submitting any case of suspected Hirschsprung's disease to operation.

We have had disappointing results from treatment by drugs, spinal anæsthetic and by operation and I have been most impressed by the short-term results which Mr. Stevens has obtained. It is, however, interesting that one child, aged 7 years, with undoubted megacolon has cured himself functionally by learning to assume the knee-elbow posture thrice daily. He expels a large amount of flatus by this method and subsequently has a bowel action. Presumably the mechanism by which this trick works is an unkninking of the rectosigmoid junction and it is so simple that it might be worth trying before operating on cases of Hirschsprung's disease.

Though bronchopneumonia with gastro-enteritis seems to be the most common cause of death in Hirschsprung's disease, it is noteworthy that two of our cases, aged 3 and 5 years, have collapsed and died within a few hours. Post-mortem examination showed in one case coincident gastroenteritis and in the other tuberculosis, but one does not expect sudden death from either of these causes after the age of infancy. This raises the question whether Hirschsprung's disease affects merely the colon or whether there is a more widespread pathology of the autonomic nervous system.

## Section of Experimental Medicine and Therapeutics

President—Professor G. W. PICKERING, M.A., M.B., F.R.C.P.

[October 19, 1948]

### The Place of the Experimental Method in Medicine

#### PRESIDENT'S ADDRESS

By Professor G. W. PICKERING, M.A., M.B., F.R.C.P.

OUR knowledge and understanding of natural phenomena, or natural science, has been won by the use of two methods, the method of observation, and the method of experiment. The method of observation records the properties of naturally occurring phenomena in the dimensions of space and time. It records such things as the shape, size and colour of objects and their spatial relations to one another, and it records events and their temporal relationship one to another. The method of experiment is the method of observation made under specified and controlled conditions. By this method the operating factors can be altered one by one, and the effects of those alterations determined. The two methods are thus in no way conflicting but are in fact complementary. It is characteristic of the method of science that it begins with simple observation and proceeds by the method of experiment, until a fully proved and documented explanation has been achieved.

The method of observation is of course very old, and is not peculiar to science. It was used by the ancient civilizations and by our own before the Renaissance, and the growth of modern science. It is a method of the highest importance to the growth of scientific knowledge, and is in fact the chief method in such sciences as astronomy and geology, where the scales of space and time are so great as to be beyond human competence to control and alter. But the method has very serious limitations. Events may happen so rarely and apparently so fortuitously that it may be difficult for any single observer to study them fully. Still more important, the factors which may be concerned in determining an event may be so complex that the method of observation alone may be quite incompetent to decide what is in fact a sequence of cause and effect, and what is an association of phenomena of a much looser kind. In such a situation two methods have been used to find a solution, the method of theoretical disputation and the method of experiment. The method of theoretical disputation was the sole method employed by the ancient civilizations and by our own up to the Renaissance. Without the corrective of experiment it is a method with a disastrous history, which has been probed with penetrating wit by Wilfred Trotter in his "Place of General Ideas in Medicine" and "Has the Intellect a Function". Perhaps the method came to its most malignant growth in the schoolmen of the late Middle Ages. To quote Lyell in his "Principles of Geology"—"The system of scholastic disputations, encouraged in the universities of the Middle Ages, had unfortunately trained men to habits of indefinite argumentations; and they often preferred absurd and extravagant propositions, because greater skill was required to maintain them; the end and object of these intellectual combats being victory, and not truth. No theory could be so far-fetched or fantastical as not to attract some followers, provided it fell in with popular notions." When I first read this passage I was irresistibly reminded of contemporary medical thought. It is, however, important to realize that this was the only method available to medicine until the dawn of science.

The alternative to the method of theoretical disputation is the method of experiment.

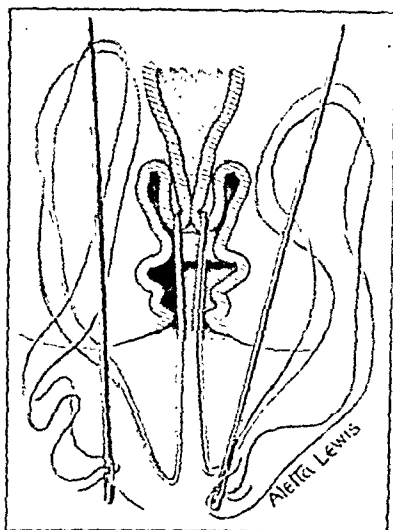


FIG. 4.

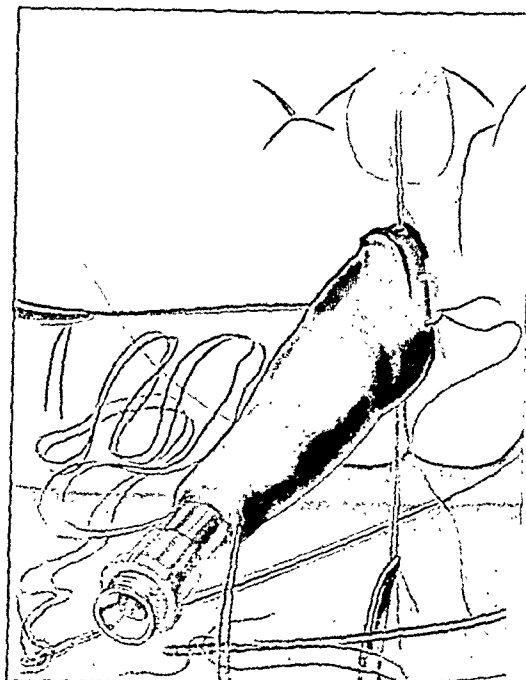


FIG. 5.

FIG. 4.—Diagram showing how traction on the silk loops produces an intussusception which further traction turns into a prolapse of the rectosigmoid outside the anus.

FIG. 5.—Showing the placing of locking sutures to hold the two layers of the prolapsed bowel together. These sutures should be placed about  $\frac{3}{4}$  in. from the actual junction of skin and bowel lining. They are inserted by highly curved needles upon the sigmoidoscope which has been reintroduced and serves to indicate when the lumen of the bowel has been reached. The suture material is strong linen.

FIG. 6.—The cutting of the double layer of bowel by means of a diathermy needle and its sewing by linen vertical mattress sutures inserted with an extra twist to hold the edges of the mucosa together. On the completion of this anastomosis the line of the sutures is allowed to retract automatically inside the anus. The original line of locking sutures may be left long in order to bring it out again should this be necessary for any reason.



FIG. 6.

of the attitude of mind of the schoolmen of the Middle Ages. It tends to be omniscient rather than admit ignorance, to encourage speculation not solidly backed by evidence, and to be indifferent to the proof or disproof of hypothesis. It is to this legacy of the Middle Ages that may be attributed the phenomenon which Wilfred Trotter used to call "the mysterious viability of the false". And it is, above all, to this habit of mind so inimical to scientific enquiry that we may trace the fact that the experimental method has found so small a place in clinical studies.

It is often said that medical education is becoming more and more scientific. The curriculum has certainly become longer and more crowded. Subject after subject has been added, nothing is taken away. And when the plea is presented that the load must be lightened before the last spark of initiative and curiosity is extinguished in the student's mind, it is said that this or that illustrates some fundamental scientific principle and must be retained as an obligatory matter for study. I often feel that we medical teachers have quite lost our sense of proportion, and our last contact with the elementary principles of education. I should like to see graven in large letters over the doorway of every medical school these words of Karl Pearson: "The true aim of the teacher should be to impart an appreciation of method and not a knowledge of facts"; for method is retained as an attitude of mind when facts have been forgotten. It is a sufficient comment on the supposed scientific basis of the medical curriculum, that during the six weary years in which the student is ground down by long hours of instruction, he has learned practically nothing of the basic methods of science. I am quite certain that his attitude of mind does not include the experimental method. In fact if a question were set in the final examination on the place of the experimental method in medicine, there would be consternation among the students. Nor is the reason far to seek. I feel equally sure that if his teachers were asked a similar question they would be in a similar plight. And if the teachers have not this attitude of mind, how can we expect it of students? That is the reason which impelled me to choose this subject. I was anxious to get my own mind clear and hoped I might interest others.

Before proceeding with our main theme it is important that we rid our minds of one common misconception. Thanks to the activities of the anti-vivisection society and others, the word experiment, particularly when used in connexion with the medical sciences, has come to mean to many the infliction of pain, suffering and even death on the unhappy subject. An experiment may mean this, but it does not necessarily do so. There are, as we shall see, many experiments which can be carried out on patients in which there is no added suffering or risk to life. Where these considerations arise, the experimenter has one golden rule to guide him as to whether the experiment is justifiable. Is he prepared to submit himself to the procedure? If he is, and if the experiment is actually carried out on himself, then it is probably justifiable. If he is not, then the experiment should not be done.

In considering the place of the experimental method in Medicine we may begin with therapeutics, for this Section was originally the Section of Therapeutics, and therapeutics is the branch of medicine that, by its very nature, should be experimental. For if we take a patient afflicted with a malady, and we alter his conditions of life, either by dieting him, or by putting him to bed, or by administering to him a drug, or by performing on him an operation, we are performing an experiment. And if we are scientifically minded we should record the results. Before concluding that the change for better or for worse in the patient is due to the specific treatment employed, we must ascertain whether the result can be repeated a significant number of times in similar patients, whether the result was merely due to the natural history of the disease or in other words to the lapse of time, or whether it was due to some other factor which was necessarily associated with the therapeutic measure in question. And if, as a result of these procedures, we learn that the therapeutic measure employed produces a significant, though not very pronounced, improvement, we would experiment with the method, altering dosage or other detail to see if it can be improved. This would seem the procedure to be expected of men with six years of scientific training behind them. But it has not been followed. Had it been done we should have gained a fairly precise knowledge of the place of individual methods of therapy in disease, and our efficiency as doctors would have been enormously enhanced. Moreover we might have learned a great deal about the nature of the diseases concerned. And it is to be noted that in this instance the use of the experimental method carries no penalties for the patient that are not inherent in therapeutics anyway. In fact by demonstrating that certain measures are actually harmful, the experimental method in the long run protects the patient.

Take for example the action of drugs. Until recently the teaching of therapeutics was subordinated to that of *materia medica* and applied pharmacology. As a result of experiments on laboratory animals of a different species, employing doses of an entirely different order, and experimenting on animals not suffering from the malady in question, the mode of action of certain drugs had been worked out. To apply these results without more ado

Here the same processes of logical thought are followed, but each idea is subjected to the scrutiny of experiment before it is accepted. It is in fact its use of experimental method which has distinguished natural science from other systems of knowledge; and it is the essence of the scientific attitude of mind that it seeks to decide doubtful points by experiment rather than by argument.

If for a moment we stand aside and look at Medicine as it exists today we find that the method of theoretical disputation still holds a dominant place. When simple observation has yielded all its results, the tendency of the vast majority of doctors is to proceed by the method of disputation, very rarely by the method of experiment. Moreover where there is a conflict between the conclusions achieved by the two methods, then it is the rule for that reached by the method of theoretical disputation to take precedence.

There are several reasons why the experimental method has been so little employed in the problems of human disease. In the first place doctors who have had an urge to advance science have found satisfaction most easily in the laboratory, away from patients and their problems. Thus have grown up, and largely through the use of the experimental method, the sciences of Physiology, Biochemistry, Bacteriology, Immunology, and Pharmacology. In recent years, both Anatomy and Morbid Anatomy have tended to become less strictly observational and more experimental. Those who become familiar with living patients and the problems they present have until recently been all engaged in practice, a strenuous and exacting life, calling for hard work and urgent decisions on a great variety of matters. Only men with exceptional originality of mind, and the greatest physical and mental vigour like Mackenzie, have been able to snatch the necessary time for reflection and the actions which it prompted from their other heavy duties. Although there have been University chairs in clinical subjects in Oxford and Cambridge and in the four Scottish Universities for many centuries, their occupants have, in general, also been so overburdened with practice and teaching that they have been in no better position than their colleagues outside the Universities. In recent years the establishment of full-time University clinical departments, and of full-time clinical research units by the Medical Research Council, offers for the first time conditions conducive to sustained scientific work.

In the second place it has been denied that the phenomena of disease as they are exhibited in human beings provide a proper field for exercising the scientific method. It has been held that the methods of science can be most profitably used in medicine in the laboratories of the so-called basic sciences of Anatomy, Physiology, Biochemistry, Bacteriology and Immunology. It is held that the proper place of science in medicine lies in the application of the principles revealed by these basic sciences to the phenomena encountered in sick people. On this view medicine consists of a series of applied sciences, applied physiology, applied pharmacology, applied immunology and the like. I imagine that this view would seldom be seriously presented on paper nowadays. Nevertheless the view persists and is widespread and consciously or unconsciously influences policy. No branch of science can profitably be pursued in isolation. It cannot advance without borrowing freely the ideas, the principles, the data and the techniques of other and related branches of scientific enquiry. Clinical Science must lean heavily on all the Biological Sciences, of which it is indeed one, as well as on Chemistry and Physics. No one could be more sensible than I am of the contributions of Physiology, Biochemistry, Bacteriology and Pathology to our understanding of the processes of disease. But it is of the very essence of science that phenomena cannot be adequately understood and explained unless they are themselves studied by the scientific method. The phenomena of disease in man must be studied by the scientific method to be understood. Moreover just as clinical science is stimulated by other branches, so physiology, biochemistry and pharmacology are stimulated by clinical science.

The third reason why the experimental method has in the past been applied so seldom to clinical studies is historical, and is to my mind the most important. In all peoples and at all times the sick seek relief from those who profess, rightly or wrongly, to be able to help them. From the very earliest times there has existed a systematized body of opinion as to the cause of disease, and its prevention. Even when Harvey made his great discoveries to the theoretical basis of medicine consisted of a small number of observed facts obscured by a large amount of speculation derived from the schools of logic and metaphysics. Much of what would no doubt then have been regarded as the fundamental principles of medicine has since proved to be demonstrably false and has been discarded. Much of therapeutics such as blood-letting, purging and starvation we now recognize to have been positively dangerous. But one cannot easily break with habits of thought, particularly in a subject like medicine when the licence to practise is only granted to those of the rising generation who subscribe and assent to the views held by an earlier generation who had been themselves subjected to the same process of screening. It is to the long and exacting curriculum, fortified with a series of awesome tests, that must be attributed the extraordinary resistance of medicine to new methods and habits of thought. Modern medicine still preserves much

and at the sight of such wonderfully complicated and colourful apparatus, suggesting that here indeed is medical science in its fullest bloom.

Much could be said of the place of the experimental method in Surgery. Surgeons perform on living men many of the operations that experimental physiologists perform on laboratory animals. But whereas the experimental physiologist is chiefly interested in his operation as a means of finding out some aspect of function, surgeons in general are more interested in the operation and less in its detailed effects. An enormous volume of information bearing on human physiology and pathology must have been wasted because the detailed effects of operations have gone unrecorded and unpublished. There have, of course, been notable exceptions, amongst whom one may cite Kocher whose observations on removal of the thyroid mark the beginnings of endocrinology. There are few aspects of clinical science that offer so fruitful a field for the use of the experimental method as surgery. For every operation is in fact an experiment; and the surgeon has available to him all the techniques that can be used by the physician in addition to his own method. Judged solely as a form of therapeutics surgery is again a most suitable field for the scientific method. We may take an example. An operation has been devised and many times performed to increase the blood supply to the heart in angina pectoris and coronary thrombosis. Its value has never been conclusively demonstrated. Yet nothing could be easier were the experimental method applied. As Wayne and others have shown patients with angina pectoris when tested under standard conditions have usually a remarkably constant exercise tolerance from day to day and from month to month. It is very easy to demonstrate in angina the effects of nitroglycerin and of anaemia. And it would be equally easy to demonstrate the effects of surgery if there are any. But this has never been done. Again, take the effect of sympathectomy in hypertension. This operation probably has a beneficial effect in some cases, but how often and in what circumstances is hard to judge. For those who have studied and published large series have done no controls. They rely on what other people have said about the natural history of the disease. Thus two important sources of error have never been ruled out, namely sampling errors and the subjective errors of different observers.

We may now consider another large division of clinical science, that concerned with mechanism. This deals with the way in which the functions of the body are altered in disease, and the way in which symptoms and signs arise. It is this aspect which is sometimes called applied physiology, a term which has led to the same kind of abuse as we have seen in the application of pharmacology to therapeutics. As it has been done in the past, it was bad science and led to bad medicine. Thus disordered action of the vasomotor nerves has been held responsible for every kind of malady affecting the peripheral vessels, for example Raynaud's disease, acrocyanosis, thromboangitis obliterans and hypertension. This was done not by careful study of the maladies themselves, but by applying so-called physiological principles. Now the proper study of this aspect of clinical science calls not so much for the application of the principles of physiology, but for the methods. In particular it calls for the experimental method, which, in the study of living organisms, has so long been developed and perfected by physiology. Applying the methods rather than the principles of physiology to these problems of the peripheral circulation showed not only that the hypothesis of overaction of the vasomotor nerves was unsupported by evidence, but also that the principles of physiology were found wanting. One of the results of this work was the rediscovery of renin which physiology had first unearthed and then buried for forty years.

In a recent article Witts has expressed doubts as to whether this is a particularly rewarding field for clinical research. He prefers the method of animal experiment more particularly directed to problems of causation. It is true that work on the mechanism of disease in man is less likely to produce top-headline discoveries than work directed to causation or therapeutics, and it will probably, therefore, provide little incentive or satisfaction to those who desire to be in the public eye. But the work must be done, because there is no other way in which the questions can be answered. And these questions are important because an understanding of mechanism is often of the greatest value both in the diagnosis and management of disease. Unless a doctor has some understanding of mechanism, he is at a loss whenever he meets a patient exhibiting phenomena a little different from those to which his rule-of-thumb methods apply.

There remains to be considered the problem of the cause of disease. As we review the manner in which our knowledge of causation has been acquired, it will be seen that the contribution made by the scientific method in medicine has been a disappointing one. For it is much more convenient for the doctor, he is more comfortable with his patients, if he has convinced himself that he knows not only what disease the patient has, but how and why he has acquired it. Such a state of mind does not allow the evidence to be enquired into for often it does not exist. Even now there is no definite evidence as to the causation



to the treatment of disease in man is a procedure so full of fallacies as to need no comment. Yet it was held to be scientific. I was taught that iron and arsenic each had a specific effect on blood formation in man, and as a student and house-physician I saw nearly all patients with anæmia treated with a mixture containing 5 grains of iron and ammonium citrate, 2 minims of liquor arsenicalis, and other ingredients to supply taste and colour, which were given long Latin names. This was a time-honoured treatment used in my hospital and generally in this country for many years. I never saw any improvement in anæmia result from this treatment, though the patients were no doubt pleased to be seen from time to time by a considerate doctor. We now know as a result of applying the experimental method that the dose of iron used was quite inadequate, that there is a very common form of anæmia which responds readily to adequate dosage of iron, and which is in fact due to iron deficiency. As a result of applying the experimental method, we are not only now able to help patients that we could not help before, but by having learned the specific nature of the malady we are now able to prevent it in people who would have probably developed it but for our intervention. As far as I know arsenic has never been shown to benefit any form of anæmia.

Another example of the application of the experimental method in the field of anæmia is the use of liver in pernicious anæmia. It is indeed a fortunate thing for those destined to suffer from this malady that the use of liver in pernicious anæmia found in Minot a man with the scientific attitude of mind. For Minot and Murphy demonstrated that the rather complicated diet they first used produced remissions that were in frequency and size altogether outside the spontaneous remissions of the disease. By applying the experimental method Minot and his colleagues showed that liver was in fact the active substance, and that the essential principle could be prepared in a form suitable for parenteral injection. By the same method Castle later showed that the inherent defect lay in the stomach, and by his work and that of Sturges and Isaacs and others a new substance was added to therapeutics. The use of liver in pernicious anæmia was a piece of very bad applied pharmacology. For the experiment was prompted by Whipple's earlier studies showing that liver had a powerful effect on blood regeneration in post-hæmorrhagic anæmia in dogs. Regarding therapeutics as an "applied science", it would have been correct to use liver in post-hæmorrhagic anæmia in man; unfortunately it happens to be inert.

This work endowed us with two powerful therapeutic agents, provided they are used for the appropriate specific defects. Iron has no action on the defect cured by liver and vice versa, and in each instance the agent has to be administered for many years. If anything were needed to show the futility of our present educational system it can be found in the common practice in hospitals, consulting rooms and homes of administering both these drugs at the same time to anæmic patients. This is not merely a waste of public money, but it confuses the doctor as to the nature of the patient's disease. And it shows how little his six years of so-called scientific education has done for the average doctor.

Many classes of drugs could be used to illustrate the point further. Reference may be made to Witts' article on ritual purgation, and Alstead's articles on expectorants and the use of bismuth in the treatment of peptic ulcer. In fact, as I look back on the system of therapeutics on which I was brought up I see that most of the prescriptions we used were more or less inert, a few were definitely harmful, some were probably beneficial, but we had little knowledge of dosage. Much of this useless and confused material is still employed to crush the student's mind. He is not taught to observe the effects of these substances and to analyse them. If he were he would realize how much of their alleged effect is due to suggestion. And this realization, a realization that a doctor may be helpful to his patients even when he knows that he has no active drug at his disposal would make him a better doctor, because a man who knows what he is doing, can usually do it better than one who does not. I believe that therapeutics is the ideal vehicle for making the student familiar with the experimental method, and it should be taught to the student essentially as an experimental science, when there are enough teachers with the right attitude of mind and sufficient understanding of the patient and his problems to make this possible. In this way the subject would become much more exciting to the student and of infinitely greater educational value.

Physiotherapy is a therapeutic department that occupies more and more space in our hospitals; employs more and more people, and costs more and more money. As a form of therapeutics it is of course well adapted for the use of the experimental method, but so far as I am aware this has not yet been applied. One is tempted to wonder whether physiotherapists are afraid that enquiry would show their methods to have a very restricted sphere of usefulness, or whether it is because the scientific method has not yet penetrated to this speciality. Many patients enjoy and value the treatment they receive, but I am quite uncertain whether the value comes from the specific measures employed, or from the uplift that their souls receive at the hands of the capable, enthusiastic and attractive female staff.

## Section of Medicine

President—Sir ADOLPH ABRAHAMS, O.B.E., M.A., M.D., F.R.C.P.

[November 23, 1946]

### DISCUSSION ON CHRONIC DIARRHŒA, EXCLUDING TROPICAL CAUSES

Dr. E. R. Cullinan: Classification of Chronic Diarrhœa.

*Introduction.*—Chronic diarrhœa (non-tropical) is an important but too often neglected symptom. Lengthy lists in textbooks of its possible causes are many, but papers analysing cases seen in practice are few. Twenty-five years ago Ryle (1924) described various types of chronic diarrhœa in 54 cases seen in this country. His classification was largely anatomical. More recently Bockus (1944) gave an ætiological classification of cases seen in Philadelphia. He put the first four causes of diarrhœa in order of frequency as being diarrhœa of nervous origin, chronic ulcerative colitis, carcinoma of the colon, and gastrogenous diarrhœa.

The following is an analysis of 99 patients whose presenting and often sole symptom was chronic, intermittent or recurrent diarrhœa. All the patients have been under my care in St. Bartholomew's Hospital, the Gordon (Westminster) Hospital, or privately during the last three years. The clinical groups into which these patients fell is shown in Table I.

TABLE I.—FINDINGS IN 99 PATIENTS SUFFERING FROM CHRONIC DIARRHŒA  
(in order of frequency)

|                                         | Cases    |
|-----------------------------------------|----------|
| (1) Chronic idiopathic colitis .. ..    | 41       |
| Whole colon .. ..                       | 12 cases |
| Middle and distal .. ..                 | 3 cases  |
| Distal .. ..                            | 21 cases |
| Regional .. ..                          | 5 cases  |
| (2) No organic cause found .. ..        | 35       |
| (3) "Post-dysenteric" .. ..             | 7        |
| (4) Carcinoma of rectum and colon .. .. | 5        |
| Rectum .. ..                            | 4 cases  |
| Colon .. ..                             | 1 case   |
| (5) Flagellates .. ..                   | 4        |
| <i>Giardia lamblia</i> .. ..            | 3 cases  |
| <i>Trichomonas hominis</i> .. ..        | 1 case   |
| (6) "Muco-membranous colitis" .. ..     | 3        |
| (7) Thyrotoxicosis .. ..                | 1        |
| (8) Pancreatic disease .. ..            | 1        |
| (9) Idiopathic steatorrhœa .. ..        | 1        |
| (10) Tuberculous entero-colitis .. ..   | 1        |
|                                         | <hr/> 99 |

These groups are not reviewed here in detail, and only a few remarks are made about each. Particularly, discussion about etiology and treatment has been largely omitted. It should be said, however, that the patients were thoroughly investigated. In addition to the history and clinical examination all or most of the following investigations were made: macroscopic

of such common diseases as peptic ulcer and rheumatoid arthritis. So it was that Lind's beautiful experiments on human scurvy, which should have laid the foundations of our knowledge of deficiency disease a century and a half before this came from the laboratory were blotted out by verbiage and speculation. So again the germ theory of disease had to await discovery by a non-medical scientist in Pasteur, despite Jenner's experimental demonstration of the transmission of cowpox and its protective action against smallpox. How a general practitioner with the scientific outlook can add to knowledge of causation has been shown in recent years by Pickles who first fixed the incubation period of catarrhal jaundice and by inference its infective nature.

Now it is a matter of no small importance when wrong ideas of causation are held. To quote Trotter in "The Place of General Ideas in Medicine":

"Then there is John Brown, whose life coincides roughly in time with that of Hunter, and who was the author of the famous Brunonian system. This product of reason is said to have been remarkably complete and consistent; it divided diseases into sthenic and asthenic, and treated them respectively with opium and alcohol, drugs to which Brown himself, less tough than his system, early succumbed.

"The observation of clinical facts would seem to be a pursuit of the physician as harmless as it is indispensable. Reason, however, could scarcely stop at so elementary a phase as this, and it seemed irresistibly rational to certain minds that disease should be as fully classifiable as are beetles and butterflies. This doctrine found its most eminent cultivator in the great Sydenham but bore perhaps its richest fruit in the hands of Boissier de Sauvages. In his 'Nosologia Methodica', published in 1768, the year of Hunter's appointment to St. George's, this Linnaeus of the bedside grouped diseases into ten classes, 295 genera, and 2,400 species. Towards the end of our period these particular developments met an opponent in Broussais, who lived till Lister was 11 and Pasteur 16. For Broussais disease in the sense of the nosologist had no existence. Diseases were for him consequences of local irritation and resulted in gastroenteritis, which was the essential pathological lesion of all maladies. Broussais' quality is shown by his aphorism: 'La nature n'a aucun pouvoir de guérison naturelle'; believing this, he knew that recovery depended solely on the exertions of the physician. Since the condition he had to contend with was always an irritation and could be met by reducing the patient, he set himself to starve and bleed with a dreadful rigour. The lapse of a hundred years has made this doctrine seem no more than gruesome balderdash, but it was not without plausibility for the contemporary world. In fact, no less a surgeon than the great Dupuytren was a believer, and was accustomed to add to his mere surgical powers of reducing his patients the sterner measures of his colleague.

"If these instances give a fair sample of what the intellect was doing for medicine for 200 years, it is not perhaps surprising to find Hunter about the middle of that period exclaiming impatiently, 'Why think?'."

Starvation and the like were practices that caused much unnecessary suffering and death and were derived from these ideas about causation. In the present day we have witnessed the indiscriminate removal of teeth, tonsils and other not wholly indispensable organs, sacrificial offerings on the altar of the hypothesis of focal sepsis.

No doubt in the future as in the past animal experiment will contribute very largely to our knowledge of causation. Nevertheless any idea so arising must be proved or disproved on man before it can be accepted. In this process the experimental method is quite indispensable.

One last word. Much has been written of the contrast and the conflict between the art and science of medicine. It is quite true that a man may be a good doctor but a poor scientist and vice versa. Yet there is nothing irreconcilable between the two. The art of medicine depends on a familiarity with disease, its manifestations and natural history and a capacity to understand people and give wise counsel. These characteristics are assets rather than liabilities to the man of science, save in one respect, that his counsel is sought so frequently that he has neither time nor energy left to pursue his scientific work. For no good scientific work is ever accomplished except by the sweat of the brow.

My view is, therefore, that a fuller acquaintance with the nature and usefulness of the experimental method is necessary not only for the few research workers but for at least a substantial part of the medical profession. It is not enough to have our Harveys, our Linds and our Jenners when their contributions are buried in a mass of wordy speculation, medicine's legacy from the schoolmen of the Middle Ages. Moreover the processes by which exact knowledge is gained and understanding developed by the individual and by organized science are essentially the same. The experimental method is not peculiar to the laboratory. It can be used in the garden as the abbot Gregor Mendel showed, in the field as Darwin showed, and in the clinic. Its use implies an attitude of mind that seeks to discover and verify facts and to understand them. I cannot believe that such an attitude of mind is out of place in a doctor even if he devotes his life to the practice of his profession. And I think it is our duty as teachers to try and inculcate this attitude.

upset, perhaps a most dramatic one, and less often to cold, or errors of diet, or other factors. When the lesion affected the whole colon there was fever, toxicity, dehydration, and emaciation with the passage of frequent foul and fluid stools with intermingled blood and pus. When the distal colon alone was affected the illness was marked more by grave anaemia. The blood was less well intermingled with the faeces but might be profuse. Sometimes, in this distal type, there was no diarrhoea, and might even be constipation. Even so, there were still frequent motions consisting of blood and mucus. Then, after a period of great illness, when the patient seemed almost moribund, a most spectacular recovery would take place and health be restored. No pathogenic organism was discovered in the stools of any patient in the group. In patients who had fractional test-meals, achlorhydria or gross hypochlorhydria was found in 7 out of 8 where the whole colon was affected, and in 16 out of 28 of the total. The significance of this is discussed later.

No specific therapeutic agent has yet been found. Successful treatment still depends upon a knowledge of the natural history of the disease, expert nursing, detailed unremitting care in alleviating symptoms as they arise, and the patience, resourcefulness, and encouragement of the physician. Surgical treatment is not indicated in the uncomplicated case. Permanent central terminal ileostomy, the only operation short of colectomy, which has stood the test of time, should be reserved for cases where complications such as pericolic abscess make it essential.

The prognosis of chronic idiopathic colitis is less grave as regards life than was once thought. Of the patients in the present series, two are dead. The disease in one had a fulminant onset, the only example seen, and the patient died sixteen days later after laparotomy at which thirteen perforations of the descending colon with general peritonitis were found. The other patient also died of general peritonitis following perforation. The remaining patients are relatively well and some quite well. I agree with Monaghan (1944) that with care it should be possible to rehabilitate 75% of sufferers.

#### *Diarrhoea with no organic lesion or pathogenic agent found.*

Excluding patients suffering from chronic diarrhoea following dysentery and patients with so-called "muco-membranous colitis" this group contains 35 cases; 20 women and 15 men. It is a heterogeneous group and the cases require further study. The patients all complained of passing loose and frequent stools, perhaps with mucus, but without blood.

In some patients the diarrhoea was continuous, in others intermittent. It might occur only in the mornings, after meals, in the cold weather, or, in women, after monthly periods. In others the diarrhoea alternated with bouts of constipation and in a few it was concurrent with constipation. Defecation was sometimes urgent or precipitant, keeping the patient constantly on tenterhooks. Passage of small quantities of mucus might lead to slight but distressing incontinence. Many of the patients complained of abdominal pain or cramps, dyspepsia and lassitude, but otherwise remained in good physical health. They were seldom troubled by diarrhoea during sleeping hours. The age of onset was widely spread over the decades and most of the patients had had their symptoms for a considerable time (see Table II).

The onset was often sudden and could be dated to an incident, perhaps a particularly frightening one. After that the diarrhoea persisted. It was Æsop who said:

"The wulf shote thyres for the grete fere he had".

Excitement, worry, anxiety, fear, and fatigue from overwork were frequent factors mentioned by the patients as exacerbating causes. Also certain foods, fruits and cold weather were often blamed. In the older age-groups fear of cancer was sometimes the perpetuating irritant. Four patients aged respectively 40, 54, 60 and 70 who had had diarrhoea for several months, and one of them for two years, lost their symptoms immediately they were assured they had not got a malignant growth. Often the patients were nervous types, but they were more obviously so and more ready to tell of their anxieties than the often "inturned" and reserved patients suffering from chronic idiopathic colitis.

It seemed that many of these patients had nothing more than an unduly sensitive colon with an exaggeration of the normal physiological response. No pathogens were found in any of the stools. Allergy was never proved in any of the cases. 11 out of 30 patients who had fractional test-meals had achlorhydria or gross hypochlorhydria. There is no evidence that patients suffering from diarrhoea of the type described in Group 2 subsequently develop chronic idiopathic colitis.

#### *Note on achlorhydria or gross hypochlorhydria in Groups 1 and 2.*

Achlorhydria or gross hypochlorhydria was frequently found in patients of both Groups 1 and 2. Its role is difficult to assign. In some instances, it was associated with rapid

appearance and pathology of the stools; examination with proctoscope and sigmoidoscope; X-rays after barium enema; and nine hours after a barium meal, to see among other things, how far the meal had progressed; the time of passage of food from mouth to anus by means of a carmine-coloured meal; a fractional test meal; and blood examinations.

Chronic diarrhœa associated with chronic idiopathic colitis and chronic diarrhœa with no organic lesion or pathogenic agent discovered occurred in almost equal proportions and accounted for over three-quarters of the total number of cases in the series. It should be remarked that the cases in both these groups are psychosomatic within Halliday's (1943) definition of the term. They are bodily disorders whose nature can be appreciated only when emotional disturbances are investigated in addition to physical disturbances. Ten years ago I believed this applied to chronic idiopathic colitis and I asked Dr. Wittkower to examine 40 unselected cases. He found (Wittkower, 1938) that in 37 of them psychological abnormalities and disorders far beyond the range of individual differences in the average population antedated the initial onset of colitis. Disturbing events in the patient's life had precipitated the onset, return, and increase of symptoms more often than could be due to chance. Today this view is generally accepted. Its truth certainly applies to the cases with chronic idiopathic colitis in Group 1 of the present series. In Group 2, where no organic lesion or pathogenic agent was found, emotional factors were even more obvious. The worries, the excitements, the anxieties and the fears wove their way in and out of the histories of these patients. In both groups the patients were mostly sedentary workers of a higher educational standard than the general hospital class. There was only one manual worker among them.

#### *Diarrhœa with chronic idiopathic colitis (chronic ulcerative colitis).*

Diarrhœa associated with chronic idiopathic colitis of undetermined origin, with or without evidence of ulceration (chronic ulcerative colitis), accounted for 41 of the 99. The lesion affected the whole colon in 12 patients, but appeared to be confined to the middle and distal portions in 3, to the distal portion in 21 and to regional portions in 5. In a previous article (Cullinan, 1938) I thought that no such real division into anatomical types could be made and that one not only saw all gradations between them but that one type might change into another. Now I am less certain. A generalized type may change into a distal type, but the opposite is seldom seen. In other words, the so-called granular procto-colitis seldom becomes a generalized chronic ulcerative colitis, though the converse may be true. In all types except the regional, the lesion was maximal at the distal colon and upper rectum. The sigmoidoscopic appearances might be identical whether the whole colon or only the distal part was affected, and the presence or absence of visible ulceration bore no relation to the extent of the lesion or the severity of the illness.

The age of onset of symptoms in the majority of the patients was between 21 and 40 (Table II). There were 24 women and 17 men. The clinical features were characteristic of

TABLE II.—GROUPS 1 and 2. 76 CASES

| Age of onset (years)       | A. Age of Onset |       |       |       |       |       |       | Total |
|----------------------------|-----------------|-------|-------|-------|-------|-------|-------|-------|
|                            | 0-10            | 11-20 | 21-30 | 31-40 | 41-50 | 51-60 | 61-70 |       |
| Chronic idiopathic colitis | 0               | 3     | 15    | 16    | 3     | 3     | 1     | 41    |
| No organic cause           | 0               | 4     | 6     | 10    | 7     | 6     | 2     | 35    |

#### B. Duration of Symptoms when Examined

| Duration of symptoms (years) | Under  |     |      |       |       |       |       | Total |
|------------------------------|--------|-----|------|-------|-------|-------|-------|-------|
|                              | 1 year | 1-5 | 6-10 | 11-15 | 16-20 | 21-25 | 26-30 |       |
| Chronic idiopathic colitis   | ..     | 8   | 16   | 9     | 3     | 2     | 2     | 41    |
| No organic cause             | ..     | 10  | 17   | 6     | 1     | 1     | 0     | 35    |

this strange disorder and need not be stated in detail. The onset was sudden or insidious. Blood and mucus appeared in the stools early. It was exceptional to find a past history of long-standing chronic diarrhœa preceding the passage of blood in the stools. The illness ran a chronic course marked by relapses and remissions. It will be seen from Table II that the majority of patients had had symptoms for periods ranging from one to ten years and several for a longer time. The nature of the onset bore no relation to the subsequent severity of symptoms. The most banal beginning might have the most serious sequel. Length of remissions were irregular and unrelated to the number or severity of previous relapses. The severity of one relapse bore no relation to the severity of another. During remissions patients might remain well and show objective signs of healing. At any stage a patient might gradually or suddenly become profoundly ill. The relapses were related very often to an emotional

## REFERENCES

- BOCKUS, H. L. (1944) *Gastro-Enterology*, Philadelphia, 2, 538.  
 CULLINAN, E. R. (1938) *Brit. med. J.* (iii), 1351.  
 HALLIDAY, J. L. (1943) *Lancet* (ii), 692.  
 HARDY, T. L. (1945) *Lancet* (i), 519, 553.  
 MONAGHAN, J. F. (1944) *Gastro-Enterology*, by Bockus, H. L. Philadelphia, 2, 549.  
 RYLE, J. A. (1924) *Lancet* (ii), 101.  
 WITTKOWER, E. (1938) *Brit. med. J.* (ii), 1356.

Dr. A. Morton Gill (*in absentia*), read by Dr. Elizabeth Falle :

### Non-tropical Steatorrhœa.

With presentation of three unusual cases.

Non-tropical fatty diarrhœa may be considered under the following headings :

- I. Idiopathic steatorrhœa.
- II. Deficiency of pancreatic secretion due to (a) chronic pancreatitis; (b) pancreatic calculi; (c) carcinoma of the pancreas.
- III. Blockage of intestinal lymphatics due to (a) tuberculous mesenteric adenitis; (b) Hodgkin's disease; (c) other diseases of the reticulo-endothelial system.
- IV. Fistulæ between stomach or small intestine and colon.
 

|                                 |   |                                                                                                                                                                   |
|---------------------------------|---|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| A. Gastro-colic<br>Jejuno-colic | } | due to (a) Anastomotic ulcer; (b) Carcinoma.                                                                                                                      |
| B. Jejuno-colic<br>Jejuno-ileal | } | due to (a) Non-specific inflammatory adhesions; (b) Accidental or inevitable operative anastomosis; (c) Ileal resection; (d) Regional ileitis and diverticulitis. |

All such cases show one or more manifestations of deficient intestinal absorption, the phenomenon common to all being the absorption of less than 90% of ingested fat as measured by a fat balance test (Cooke *et al.*, 1946). All the patients lose weight. Failure to absorb certain elements in the diet may give rise to further symptoms and signs as follows. *Iron*: Microcytic hypochromic anemia; *Hæmopoietic principle*: Macrocytic anemia; *Vitamin A*: Night-blindness, xerophthalmia, toad skin, liability to respiratory infections, flat vitamin-A absorption curve; *Vitamin-B complex*: Beri-beri, peripheral neuritis, red bald sore tongue→ulceration, angular stomatitis, pellagrous skin lesions; *Vitamin C*: Scorbutic lesions (very rare); *Vitamin D*: Osteomalacia, spontaneous fractures; *Vitamin E*: Low plasma prothrombin→hemorrhagic manifestations; *Calcium*: Low serum calcium→tetany; *Protein*: Low plasma proteins→œdema.

Differential diagnosis by the macroscopic and microscopic appearances of the stools, by the percentage of fat in a dried stool, and by the degree of fat splitting has been shown by Cooke *et al.* (1946), to be unreliable. The diagnosis depends to a great extent on the previous history and on one or more of the following findings.

#### I. Idiopathic steatorrhœa.

Past history of similar attacks in childhood; barium meal "deficiency pattern", i.e. lack of intestinal feathering, with clumping of barium.

#### II. Deficiency of pancreatic secretion.

Past history of acute or subacute pancreatitis (severe epigastric pain→back). Duodenal intubation. Low or absent trypsin in duodenal juice. Serum amylase, raised (early), low or absent (late). Glucose tolerance curve, normal (early), diabetic (late). Split fat in stools, less than 70% of total fat. Jaundice. Radiological evidence of calculi.

#### III. Blockage of intestinal lymphatics.

Past history vague; diarrhœa of gradual onset; palpable mesenteric glands; calcification of mesenteric glands; enlargement or biopsy of other reticulo-endothelial tissue.

#### IV. Fistulæ.

Past history of dyspepsia, altered appetite or bowel habit, intestinal pain or previous operation suggestive. Barium meal or enema conclusive.

CASE I.—M. H., an unmarried woman of 33, was admitted to the West London Hospital in April 1948 with a history of fatty offensive diarrhœa for seven months, colicky peri-umbilical pain, abdominal distension, occasional vomiting, loss of 1 st. in weight, greying hair, and amenorrhœa. Her mother said that she had had similar diarrhœa from birth until she was 10 years old. At the age of 5 she had had tuberculous osteomyelitis of several fingers, of her left elbow and right forearm, and

passage of contents through the gastro-intestinal tract and the appearance of undigested meat and vegetable fibres in the stools. In other instances there was rapid passage as far as the distal colon and then subsequent constipation. In many others, however, there was no evidence of rapid passage. Whatever the significance of achlorhydria, there is no proof that it is a direct causative factor in the production of diarrhœa.

#### *Diarrhœa following amœbic dysentery.*

In the recent war many people who went overseas contracted amœbic dysentery. Unfortunately, there are many still suffering from the disease, and it requires vigilance and most careful examination to detect it. But there are others who had intestinal amœbiasis, assumed or proven, from which they recovered after adequate treatment, who nevertheless still have recurrent bouts of diarrhœa. Repeated search of fresh warm stools fails to reveal any parasites or cysts and the sigmoidoscopic appearances of the lower bowel are normal. 7 examples are included in the present series. None had complained of diarrhœa prior to the amœbic infestation. The cause of this syndrome is not known. The theory that it is a neurosis is unconvincing. The diarrhœa tends steadily to improve and finally disappear, and from this one might infer that it is the result of the bowel having become unduly sensitive as a result of the previous infestation. I think those of us who have had experience in warm climates of dysentery in its various forms will all agree that chronic bacillary dysentery, in contradistinction to amœbic dysentery, is extremely rarely, if ever, seen.

#### *Diarrhœa with carcinoma of the rectum and colon.*

5 cases had carcinoma of the lower bowel. The small number is no cause for complacency. The diagnosis of a growth will seldom be missed if several well-known facts are remembered. The history may be misleading. In one of the 5 cases diarrhœa started after a police dinner five months previously and was made worse by certain foods. Any change of bowel habit in middle age should always be regarded with suspicion. The presence of frank blood in the stools of an adult should spell cancer until proved otherwise. Piles are present in a large number of rectal cancers. A large number of cancers of the lower bowel, perhaps 50% are within reach of the examining finger and still more are within reach of the sigmoidoscope. The remainder may be found by X-rays.

#### *Diarrhœa with flagellates.*

In the Middle East the *Giardia lamblia* was described as the "spy of the amœba". When found in the stools it nearly always masked an amœbic infestation. However, the 3 patients in Group 5 of this series had not been overseas and repeated search failed to reveal any other parasite in the gut. The patients had intermittent diarrhœa with pale offensive stools of the small intestine type, together with dyspeptic symptoms and abdominal discomfort. In one instance there was a little œdema of the recto-sigmoid junction. The patients were much improved with atabrin. The case of *Trichomonas hominis* is included, although some people doubt whether this parasite causes symptoms. The patient, an ex-Palestine policeman, had had loose stools without blood associated with epigastric discomfort for three years.

#### *Diarrhœa with "muco-membranous colitis".*

There are only 3 examples of the old-fashioned "muco-membranous colitis" in this series. It should not really be called colitis. Hardy describes it as "this period piece; a relic of late Victorian and Edwardian epochs; a common disorder till 1914 when it disappeared". The 3 patients were women who had had symptoms for five, twenty-five and twenty-eight years. They looked in excellent physical health, complained of considerable abdominal pain, were constipated when not taking purgatives but had loose or explosive motions when doing so, and intermittently passed large quantities of mucus. They commanded immense sympathy from a variety of friends and devoted their waking lives to a contemplation of their bowels. Chronic idiopathic colitis is not a sequel of this syndrome.

#### *Diarrhœa with other conditions.*

The remaining groups consist of one case each of chronic diarrhœa with thyrotoxicosis, pancreatic disease (a rare cause of diarrhœa), idiopathic steatorrhœa, and tuberculous enterocolitis. In each instance diarrhœa was the presenting symptom.

#### CONCLUSIONS

The clinical groups of 99 patients whose presenting and often sole symptom was chronic, intermittent or recurrent diarrhœa have been described. Every patient suffering from chronic diarrhœa requires careful examination and investigation. Diarrhœa without discoverable organic cause can be diagnosed only by exclusion.

of symptoms coincided with the ileo-ileostomy, this fistula appears to have resulted from non-specific inflammatory adhesions between the ileum and rectum. One similar case has been found in the literature (Ware, 1920).

CASE III.—F. Y., an unmarried female aged 37, was admitted to the Ministry of Pensions Hospital Stoke Mandeville, in June 1948. Five years previously she had had an appendicectomy with drainage, followed by an operation one week later, for obstruction. Since then she had had diarrhoea and lost 4 st. in weight. Her stools were frequent, pale, bulky and offensive; she vomited occasionally; she had had amenorrhoea for twenty months, a sore and ulcerated tongue for three months, and constant oedema of her ankles for one month.

Examination showed a grossly emaciated woman weighing 5 st. 2 lb. Her tongue was smooth and red; the edges were raw and ulcerated. A large incisional hernia presented through an old upper mid-line abdominal scar. Her liver edge was felt five fingerbreadths below the right costal margin. This edge was smooth and firm.

On the history and signs a clinical diagnosis of jejuno-colic fistula was made.

On further investigation she was found to have 51 grammes % fat in a dried specimen of her stool, of which 84% was split. Both fatty droplets and fatty acid crystals were seen microscopically. She had a macrocytic anemia, her haemoglobin being 55%. Barium enema showed an enormously dilated lower bowel. Barium suddenly appeared in the small intestine from the transverse colon, thus confirming the clinical diagnosis.

In August 1948 a laparotomy was performed by Mr. Strang revealing a surgical anastomosis between the transverse colon and jejunum, some 12 in. from the duodeno-jejunal flexure. The jejunum was divided above and below the fistula and an end-to-end anastomosis made. The opening in the colon was closed by transverse suture. The liver was slightly enlarged but otherwise normal. She made excellent progress after operation and gained 1 st. 7 lb in one month.

This then is a case of an accidental surgical anastomosis between the jejunum and the transverse colon, an error which the most expert can make during operation for acute intestinal obstruction. Two cases of accidental jejuno-colic anastomosis have been found in the literature (Little *et al.*, 1929; Christopher, 1935).

(The cases were illustrated by slides shown at the meeting.)

Thanks are due to Mr. Harold Burge and Mr. Strang for their surgical skill; to the radiologists, biochemists, pathologists and photographers at the West London Hospital and to the Ministry of Pensions Hospital, Stoke Mandeville.

#### REFERENCES

- CHRISTOPHER, F. (1935) Vicious jejuno-colostomy with chronic ileac obstruction, *Amer. J. Surg.*, 29, 124.  
 COOKE, W. T., *et al.* (1946) Anomalies of intestinal absorption of fat, *Quart. J. Med.*, 15, 141.  
 LITTLE, W. D., ZERFAS, L. G., and TRUSLER, H. M. (1929) *J. Amer. med. Ass.*, 93, 1290.  
 WARE, M. (1920) Jejuno-colic fistula, *Ann. Surg.*, 72, 607.  
 WILKINSON, J. F. (1948) Folic acid, Part II, *Brit. med. J.* (i), 822.

Dr. J. W. Pauley: Chronic Diarrhoea.

There are four main points which I wish to put forward on this subject:

- (1) The need for a physiological classification of chronic diarrhoea.
  - (2) That patients with certain diseases of the small intestine have personality traits akin to, but mainly distinct from, those found in colitis and duodenal ulcer.
  - (3) A plea for caution before accepting Thaysen's findings on the morbid anatomy of the small bowel in steatorrhoea.
  - (4) Finally, I wish to put forward a concept that the alimentary canal be considered as a whole in anatomy, physiology and disease, and not as a series of isolated segments.
- (1) First, Ryle's anatomical classification for the chronic diarrhoeas has stood since 1924 [1] and is included with reservations by Bockus [2]. I would, however, prefer to see diseases of the alimentary tract approached as problems of disordered physiology rather than of deranged anatomy.

The difficulty and inadequacy of a physiological analysis should serve as a spur to remind us of our present ignorance and replace the easy sense of self-satisfaction sometimes engendered by the symmetry and smoothness of an anatomical classification. I would suggest that most chronic diarrhoeas can be brought under the following main heads:

- (a) Inadequate absorption (in the small intestine of water and food products, particularly fat; in the large intestine of water only).
- (b) Excessive secretion, mucus, serum and even blood.
- (c) Disordered motility of muscle, and increased irritability.



tuberculous mesenteric adenitis was said to have been found at operation for appendicitis five years ago. The mother has pulmonary tuberculosis.

A photograph taken in the spring of 1947, i.e. one year before admission, portrayed a young and attractive woman with abundant hair, whereas on admission she looked thin, pale and old; her hair was grey, scanty and lustreless. Her weight was only 6 st. She had a clean moist tongue, but a distended tympanitic abdomen. She was extremely tender in both hypochondria with guarding.

Further investigation revealed a mild macrocytic anaemia (haemoglobin 82%), a normal white cell count with a relative lymphocytosis (61% lymphocytes). There were 65.3 grammes% fat in the dried stool of which only 55% was split: microscopically, fat plaques and many fatty acid crystals were seen, but no blood, pus, Koch's bacilli or undigested muscle fibres. She had a flat oral glucose tolerance curve.

Radiographically, her chest was normal but the presence of a pancreatic calculus was queried on an abdominal film.

At this time the history of diarrhoea since birth and the poor splitting of faecal fat was thought to indicate a pancreatic deficiency. A low fat diet with pancreatic enzymes, injections of concentrated vitamins A and D, and of anahemin, were all tried without effect. Intermittently, she had exacerbations of colicky peri-umbilical pain and distension with constipation. Her temperature intermittently rose to 99° F. but she did not vomit. Eventually her symptoms became so severe that operation for possible obstruction was decided upon.

On May 22, Mr. Harold Burge did a laparotomy. The whole of the small intestine and the pelvic colon were widely dilated but there was no organic obstruction. A few soft glands were felt in the mesentery: these, on section later, showed chronic inflammatory changes only. The pancreas was not seen but was easily felt and seemed normal. The case was therefore returned to the physicians as a "medical abdomen".

These findings, together with a flat oral glucose tolerance curve, left no alternative to a diagnosis of idiopathic steatorrhoea. Folic acid was therefore given, in a dosage of 10 mg. b.d., with dramatic effect. The diarrhoea ceased, the abdominal symptoms disappeared, she gained 9 lb. in the three weeks following operation and has never looked back since.

Now, six months later, she weighs 7 st. 3 lb., her hair is returning to its original colour, she is menstruating normally, mammary and subcutaneous fat have been re-deposited, and she has a normal bowel action once daily. She continues to take 10 mg. of folic acid twice daily.

The final diagnosis was therefore idiopathic steatorrhoea, though the history of diarrhoea from birth, the possibility of tuberculous mesenteric adenitis, and the abdominal pain, were all misleading. This case again shows the fallibility of differential faecal fat estimations. Like other reported cases of idiopathic steatorrhoea associated with a macrocytic anaemia (Wilkinson, 1948), the response of the diarrhoea to folic acid has been excellent.

CASE II.—M. K., a married woman of 61 years attended the West London Hospital in August 1948. Ever since an operation for subacute intestinal obstruction at another hospital seven months previously, she had suffered from diarrhoea. She was passing a loose pale frothy motion after every meal and had a bearing-down type of lower abdominal pain especially after food. She had lost 4½ st. in weight during these seven months. She had had a subtotal hysterectomy twenty-three years before.

Examination showed a pale wasted woman, with a red, bald tongue. There was a large incisional hernia through a lower mid-line abdominal scar and a doubtful mass was felt in the left iliac fossa. On rectal examination a soft mass was present, lying to the left of a normal cervix. This did not bleed on touching.

The provisional diagnosis of a fistula between the small intestine and the colon was therefore made and further investigations confirmed it. Only the descending colon was filled during the barium enema but there was the suggestion of a tiny fistulous track running upwards from the rectum. Barium meal and follow through at two hours showed barium in the small intestine; at two and a half hours showed barium in the lower ileum and rectum. Not until four hours did it appear in the caecum. The presence of a fistula between the ileum and rectum was thus proved.

Further investigation after admission in September 1948 showed that she had a moderately severe microcytic hypochromic anaemia; a rise of total faecal fat to 39 grammes%, of which 76% was split; little evidence of undigested food in the stools and a mild recurrent *B. coli* urinary infection. Details of her operation for obstruction in January 1948 revealed that a side-to-side ileo-ileal anastomosis had been performed to by-pass three tightly matted coils of small intestine adhering to the subtotal hysterectomy scar.

In October 1948 she was operated upon by Mr. Harold Burge. He found almost all the small gut coils adherent to one another, which, when separated, showed the operative anastomosis between two coils of lower small bowel. Beyond this, two loops of small bowel formed an inflammatory mass, where they were adherent to, and communicating with, the rectum. These fistulous loops were resected leaving the previous operative anastomosis functioning. The hole in the rectum was repaired and a left iliac colostomy was performed to divert, temporarily, the faecal flow.

She is now being discharged from hospital feeling very well, free of pain for the first time in nine months and rapidly gaining weight. Her colostomy is to be closed at a later date.

This case demonstrates the importance of an accurate history, and although the onset

brought about in Crohn's disease and steatorrhœa may not be entirely due to chronic gut dysfunction. Stages in the disease process being hyperæmia, mucosal lymphœdema, motor irritability and chronic inflammatory change; mucosal states not infrequently seen through the gastroscope or at operation in duodenal ulcer (but how seldom in the post-mortem room!). Similar states can also be seen through the sigmoidoscope in colon neurosis and colitis.

As far as cœliac disease is concerned, examination of the patient when an adult may be misleading, as chronic illness in childhood is a potent factor in production of dependence and emotional immaturity. The subject therefore requires investigation in childhood by a child psychiatrist, and/or an enquiring paediatrician.

The concept that tropical sprue is related to personality traits is not altogether a new one and has in the past had some support in Holland [14, 15]. It has been said by some authors that such patients were often peculiar in character, and lacked balance in psychic as well as physical aspects.

The so-called deficiency pattern of the small intestine has puzzled many workers for a long time [16, 17, 18, 19]. It is known that coarsening of the valvulæ conniventes is almost universally present to a marked degree in cases of active steatorrhœa. The fact that it may be present with some frequency in other diseases, including colitis and duodenal ulcer and even in the apparently normal, has rightly thrown doubt on its specificity as indication of vitamin deficiency. There is evidence that emotional upsets are capable of promoting identical changes in susceptible individuals at any rate temporarily [20, 21]. I would suggest that when these emotional effects persist for a long period such changes, as already postulated, may occur in the mucosa and in late cases lead to atrophy. When this happens in the jejunum, nothing is more likely than that fat absorption should be impaired, possibly by mechanical interference with particulate fat absorption through the brush border of the intestinal epithelium [22].

(3) This hypothesis has the additional advantage that it is to some extent in accord with the carefully recorded findings of older workers [23, 24, 25, 26, 27] in steatorrhœa and sprue, but it cuts across the present-day teaching which dates from Thaysen's work in the early 1930s [28, 29]. I have read Thaysen's papers carefully and his arguments to me are confusing, and somewhat unconvincing. He bases his observations on the post-mortem material of two cases of his own (one sprue and one non-tropical sprue) and a rather one-sided view of the literature. I believe that many reading Thaysen will find his case non-proven, and until it is we should keep our minds open on the matter of mucosal change occurring in the steatorrhœas which may well be more apparent in life than after death.

(4) Finally I believe one of the greatest hindrances to a better understanding of gastrointestinal disease lies in the fact that we have been taught to look upon the gut as a series of distinct parts. Generations of medical men have thought proctitis as necessarily different in aetiology from colitis; total colitis as separate from segmental colitis; and right-sided colitis involving the terminal ileum as different from terminal ileitis with extension to the caecum and colon. We know that many cases of Crohn's disease progress to total colitis, we know that many of them have had appendicitis (and I have heard recently of a number having had duodenal ulcer). Steatorrhœas may have colitis, and I have one with a Plummer-Vinson's syndrome, while duodenal ulcers are sometimes associated with peptic esophagitis.

The following case illustrates the need for looking at the intestinal tract as a whole. A man suffered from dyspepsia from 1918 to 1928 when he had a perforated gastric ulcer. On return from convalescence an appendix abscess arose. He continued to have dyspepsia on and off until 1942 when he was X-rayed and shown to have a duodenal ulcer. In 1945 he had a partial gastrectomy for duodenal ulcer, and this was followed in eighteen months by subacute obstruction caused by the last 9 in. of the terminal ileum being bound down in the pelvis. No further comment on its state was available, but it may well have been Crohn's disease. An ileo-transverseostomy was done short-circuiting about a foot of ileum, he has since had steatorrhœa with anæmia, hypoproteinaemia and œdema. His psyche did not escape examination!

To summarize: I would prefer a physiological rather than an anatomical approach to the classification of diarrhœa. An account has been given of the finding in certain diseases of the small intestine of personality traits similar to those found in duodenal ulcer and colitis. I would suggest that Thaysen's findings on the post-mortem appearances in steatorrhœa require confirmation, and that we might with advantage consider the diseases of the alimentary tract broadly in relation to the whole gut rather than as isolated problems.

My thanks are due to the many members of the Staffs of St. Mark's, Central Middlesex, and Middlesex Hospitals who have allowed me to interview their patients.

In many conditions more than one of these factors will be at work. Bockus, in a recent survey [3] of the relative frequency of the types of chronic diarrhoea occurring in hospital and private practice in America, heads the list with diarrhoea of nervous origin followed by ulcerative colitis. My experience at a teaching hospital is in accord with this, but perhaps more convincing is the fact that I have also found a similar incidence with the unselected material of a district hospital (Central Middx. Hosp.).

(2) These observations are based on a study of ulcerative colitis over the past two and a half years. 171 colitis patients have been seen and investigated to date at three hospitals, namely, Middlesex 91, Central Middx. 41, St. Mark's 39.

Briefly my finding in this study is that the cause of colitis is psychogenic, and that it occurs when stress affects people with a clearly defined personality. My view of that personality differs only slightly from that described by Cullinan and Wittkower in 1938 [4] and not at all from such writers as Ruesch [5] and Groen [6].

In the last 100 cases I have only once failed to find a positive psychiatric history and that in a man I neglected to interview out of the ward. May I remind you again of the main points in this personality? They are complete dependence, emotional immaturity, lack of normal adult expression, complete lack of aggression, deep narcissism, extreme sensitivity and an invariable tendency to brood or sulk for long periods over real or imagined wrongs or insults. Such a personality occurred five times in a control series of 86 radiotherapy patients.

If one is in doubt as to the ability of emotion to affect the bowel, one has only to cast one's mind back over the years, and even if not affected personally, the cathartic effect at school of the big match or steeplechase on others can hardly have been forgotten.

In the medical world, however, it was Drury, Florey and Florey [7] in 1929 who accidentally noted the reaction of the mucosa of an explanted dog's colon to sudden noise. In 1939 Lium [8] carried these observations further. He demonstrated that a muscular organ such as the colon could damage itself following spasm with submucous oedema and hæmorrhages induced by para-sympathetic stimulation and para-sympatheticomimetic drugs. Lium also pointed out that the ulcers in the colon of patients with ulcerative colitis were limited to the lines of the long muscle bands or *tæniæ coli*. Complete understanding of the mechanism of ulceration in colitis has yet to be achieved. From frequent sigmoidoscopic studies in many patients in various phases of activity, it would seem that hyper-vascularity, followed by oedema of the mucosa, renders it liable to superficial abrasion. These changes occur at times of inner emotional tension in patients with the personality already described.

If the process continues, secondary infection with local bowel organisms may occur.

The extent of the part played by nerves or humoral agencies in the link between psyche and soma is not yet known and today the most complete piece of work on the effect of the emotion on any part of the gut remains Wolf and Wolff's observations on "Tom" [9]. Similar, but less convincing, findings have been recorded on the [10, 11, 12] lower bowel. These taken together, however, provide a fairly clear-cut picture. In this respect I have so far confined my own observations to gut motility in relation to emotion.

This brings me to the second part of my paper. A little over six months ago I interviewed a woman whose symptoms were those of low-grade colitis and who had had a proven Crohn's disease operated on four years previously. It was not too great a surprise when I found that her personality bore a very close relationship to the colon personality and that there were the usual provocative factors. Since then I have seen a further 10 cases of proven Crohn's disease. These too have shown the same personality traits. More recently all of 10 cases of idiopathic steatorrhea, 4 cases of chronic relapsing amœbiasis and possibly a Whipple's disease have fallen into the same group.

Those patients with lesions mainly affecting the small intestine appear to fall psychologically as well as anatomically between the personality found in colitis and that found in duodenal ulcer. For example, the degree of aggression and compensatory striving for security commonly seen in ulcer patients was not so evident.

I cannot of course go further into this at this stage, but this finding seems important as it tends to link together conditions hitherto considered as very distinct entities.

If further cases confirm my findings in chronic amœbiasis (and there is already a similar case recorded by Crede and others [13] in the current number of *Psychosomatic Medicine*), the long mystery and paradox of the symptom-free cyst passer in relation to the chronic amœbic invalid may be at an end. Although not excluding a secondary agent such as a ubiquitous virus or the tubercle bacillus, there seems no reason to suppose that the changes

lung; (3) the production of an inexpandible lower lobe. The following are responsible for their occurrence in the great majority of cases: (1) The induction of pneumothorax in cases with recent dense exudative disease with toxæmia; (2) errors of technique, (a) in keeping up pneumothoraces in cases with unclosed cavities and in cases with apical adhesions in which fluid appears early, (b) injudicious adhesion section, (c) lack of continuity of treatment.

Every therapeutic pneumothorax should be a real trial pneumothorax. It should be remembered that if the pneumothorax is abandoned at once, it can usually be reintroduced if required with the same result as before. If there are very extensive adhesions to a cavitated area, and especially if the lower part of the lung is not firmly attached to the diaphragm, the pneumothorax should be considered to have failed and further air only introduced so that additional steps can be taken. In the cases, in spite of the occasional success attending extensive cauterization, even inspection of the adhesions should not be attempted. Human nature being what it is, there are few thoracoscopists who will not occasionally attempt too much; the relatively high proportion of occurrence of troublesome fluid, either immediately following the operation or later in the treatment, will in the end more than counterbalance the occasional dramatic successes. Usually the immediate temporary interruption of the phrenic nerve and institution of a pneumoperitoneum should be undertaken. This should be done before the air has been absorbed from the pleural cavity as the results will be better than if the absorption of the air is awaited. Where the adhesions look less unpromising, the pneumothorax should be continued at a definitely negative pressure with small frequent refills. No pneumothorax should be kept up if measures to close a cavity have failed. Apart from the cases where the cavity-bearing area is completely adherent, and thus the pneumothorax has no effect upon it, I can only recall one case in which a pneumothorax maintained in the presence of an open cavity did not eventually produce disaster. In addition, if a pneumothorax is kept up with a cavity for more than a few months, the attempt to allow re-expansion prior to a thoracoplasty will lead to an aspiration spread into the other lung in a high proportion of cases. It must also be remembered that the apparent improvement in health which so often follows a pneumothorax in no way obviates the risk of a spread from an unclosed cavity. Failure to remember this leads to the postponement of alternative methods of collapse therapy, and disastrous results due to this is one of the causes of the fall in popularity of therapeutic pneumothorax.

In support of these statements I will show figures from three sources where I am responsible. In the Brompton clinic I exercise merely general supervision but the regular supervision and refills are done by a series of Chief Assistants and House Officers. In the Private and St. Bartholomew's Hospital Group I do all the work myself. In the Brompton group the patients have had their pneumothoraces instituted in many places and were taken on as they attended the clinic, i.e. many with pneumothoraces which in my opinion were unsatisfactory. In the other two series either the pneumothoraces were started by myself or I approved of their condition before taking them over. The series refers only to cases who were thought fit for discharge from the institutions where the pneumothoraces had been started, i.e. ambulant.

TABLE I

|                   | No. of<br>A.P.s | Empyemata | Empyemata<br>with<br>unclosed<br>cavities | Result                                 | Unclosed<br>cavities<br>without<br>empyemata | Result                                                    |
|-------------------|-----------------|-----------|-------------------------------------------|----------------------------------------|----------------------------------------------|-----------------------------------------------------------|
| Brompton Clinic   | 217             | 44<br>20% | 18                                        | D.16<br>A. & W.<br>with $\theta$ 2     | 18                                           | D.16<br>A. & W.<br>with $\theta$ 2                        |
| St. Bart's Clinic | 61              | 3<br>5%   | 3                                         | D.3                                    | 5                                            | D.3<br>A. & W.<br>with $\theta$ 2                         |
| Private Practice  | 45              | 5<br>11%  | 3                                         | A. & W. 1<br>A & W.<br>with $\theta$ 2 | 3                                            | A. & W.<br>with $\theta$ 2<br>D. ( $\theta$<br>refused) 1 |

Empyemata are defined as having fluid which is turbid or thicker.  $\theta$  denotes thoracoplasty.

The figures show that in the Brompton series the percentage of empyemata (20%) is very high but much lower in the other series where selection was better and treatment carried out by one individual. The empyema cases with cavities and the cavity cases even without empyemata all died unless a thoracoplasty was performed with one exception in which the cavity was closed by the pressure of the increasing pus which was too thick to aspirate.

The early stages of the work on colitis were carried out as Will Edmunds Research Fellow (Royal College of Physicians).

## REFERENCES

- 1 RYLE, J. (1924) *Lancet* (ii), 101.
- 2 BOCKUS, H. L. (1944) *Gastro-Enterology*. Philadelphia, 2, 536.
- 3 — (1944) *Gastro-Enterology*. Philadelphia, 2, 538.
- 4 CULLINAN, E. R. (1938) *Brit. med. J.* (ii), 1351; WITTKOWER, E., *Brit. med. J.* (ii) 1356.
- 5 RUESCH, J. (1946) *Chronic Disease and Psychological Invalidism*. Psychosomatic Medicine Monographs, No. 9, New York.
- 6 GROEN, J. (1947) *Psychosom. Med.*, 9, 151.
- 7 DRURY, A. N., FLOREY, H., and FLOREY, M. E. (1929) *J. Physiol.*, 68, 173.
- 8 LIUM, R., and PORTER, J. (1939) *Arch. int. Med.*, 63, 210.
- 9 WOLF, S. G., and WOLFF, H. G. (1943) *Human Gastric Function*. London.
- 10 WHITE, B. V., Jr., and JONES, C. M. (1938) *New Eng. J. Med.*, 218, 191.
- 11 FRIEDMAN, M. H., and SNAPE, W. J. (1946) *Gastroenterology*, 7, 574.
- 12 ALMY, T. P., and TULIN, M. (1947) *Gastroenterology*, 8, 616.
- 13 CREDE, R. H., ROSENBAUM, M., and FEWIS, E. B. (1948) *Psychosom. Med.*, 10, 223.
- 14 SCHÜFFNER, W. A. P., and SNYDERS, E. P. (1928) *Verh. Ges. Verdau. StoffwechselKr.*, 8, 135.
- 15 KOOLEMANS BEIJEN, G. J. W. (1928) *Verh. Ges. Verdau. StoffwechselKr.*, 8, 148.
- 16 MACKIE, T. T., MILLER, D. K., and RHOADES, C. P. (1935) *Amer. J. trop. Med.*, 15, 571.
- 17 GOLDEN, R. (1941) *J. Amer. med. Ass.*, 117, 913.
- 18 RUFFIN, J. M., BAYLIN, G. J., and CAYTR, D. (1945) *Gastroenterology*, 4, 289.
- 19 GLASS, W. H. (1948) *Amer. J. digest. Dis.*, 15, 297.
- 20 GOLDEN, R. (1941) *Radiology*, 36, 262.
- 21 KEKWICK, A. (1947) Personal communication.
- 22 FRAZER, A. C. (1946) *Physiol. Rev.*, 26, 103.
- 23 FABER, K. (1904) *Arch. VerdauKr.*, 10, 333.
- 24 JUSTI, K. (1913) *Arch. Schiffs- u. Tropenhyg.*, 17, 505.
- 25 MANSON-BAHR, P. (1915) Report on researches on Sprue in Ceylon 1912-1914. London.
- 26 — (1924) *Lancet* (i), 1148.
- 27 MACKIE, F. P., and FAIRLEY, N. H. (1929) *Indian J. med. Res.*, 16, 799, 827.
- 28 THAYSEN, T. E. H. (1931) *Trans. R. Soc. trop. Med. Hyg.*, 24, 539.
- 29 — (1932) *Non-tropical Sprue*. London.

[January 25, 1949]

## DISCUSSION ON THE PLACE OF ARTIFICIAL PNEUMOTHORAX IN THE TREATMENT OF PULMONARY TUBERCULOSIS

Dr. F. H. Young (*Précis*): I find by reference to the *Proceedings of the Section*, 14, 15, that this subject was last discussed in 1921, twenty-seven years ago. There is still no general agreement (1) whether to use this method of treatment in individual cases, (2) how to handle details of treatment. It will, however, I think be generally agreed that apart from the potentiality of certain antibiotics, the selective collapse produced by the ideal pneumothorax overcome the tuberculous process in his lungs, provided that all complications could be avoided. Since 1921, therapeutic pneumothorax has had a vogue which was certainly excessive, but lately the balance has swung the other way and some authorities seem to regard it as a dangerous proceeding which should only be used in exceptional cases. In my opinion this is a retrograde step. The trouble has been that the technique seems so easy that it is carried out by inexperienced workers who do not understand either the proper selection of cases or the finer points of its conduct.

It is now accepted that the following types are unsuitable for artificial pneumothorax even if possible: (a) Cases with dense fibrotic disease especially of the upper zones. In these a primary thoracoplasty is preferred provided that it is not otherwise contra-indicated. (b) Cases with active tracheobronchitis within the limits of bronchoscopic vision unless a subsequent pneumonectomy can be envisaged. Even if only a lobar bronchus is involved a subsequent spread may lead to permanent collapse of the whole lung. This also applies to the cases in which giant tension cavities are present which are undoubtedly produced by tracheobronchitis. Apart from these two types, if collapse therapy is indicated, a trial pneumothorax would be considered in all cases where the respiratory reserve is sufficient if all complications, especially pleural, could be avoided.

The main complications are threefold: (1) the occurrence of tuberculous empyema with or without a bronchopleural fistula; (2) bronchogenic spreads of disease mainly to the other

lung; (3) the production of an inexpandable lower lobe. The following are responsible for their occurrence in the great majority of cases: (1) The induction of pneumothorax in cases with recent dense exudative disease with tubercula; (2) errors of technique, (a) in keeping up pneumothoraces in cases with unclosed cavities and in cases with apical adhesions in which fluid appears early, (b) injudicious adhesion section, (c) lack of continuity of treatment.

Every therapeutic pneumothorax should be a real trial pneumothorax. It should be remembered that if the pneumothorax is abandoned at once, it can usually be reinduced if required with the same result as before. If there are very extensive adhesions to a cavitated area, and especially if the lower part of the lung is not firmly attached to the diaphragm, the pneumothorax should be considered to have failed and further air only introduced so that additional steps can be taken. In these cases, in spite of the occasional success attending extensive cauterization, even inspection of the adhesions should not be attempted. Human nature being what it is, there are few thoracoscopists who will not occasionally attempt too much; the relatively high proportion of occurrence of troublesome fluid, either immediately following the operation or later in the treatment, will in the end more than counterbalance the occasional dramatic successes. Usually the immediate temporary interruption of the phrenic nerve and institution of a pneumoperitoneum should be undertaken. This should be done before the air has been absorbed from the pleural cavity as the results will be better than if the absorption of the air is awaited. Where the adhesions look less unpromising, the pneumothorax should be continued at a definitely negative pressure with small frequent refills. No pneumothorax should be kept up if measures to close a cavity have failed. Apart from the cases where the cavity-bearing area is completely adherent, and thus the pneumothorax has no effect upon it, I can only recall one case in which a pneumothorax maintained in the presence of an open cavity did not eventually produce disaster. In addition, if a pneumothorax is kept up with a cavity for more than a few months, the attempt to allow re-expansion prior to a thoracoplasty will lead to an aspiration spread into the other lung in a high proportion of cases. It must also be remembered that the apparent improvement in health which so often follows a pneumothorax in no way obviates the risk of a spread from an uncollapsed cavity. Failure to remember this leads to the postponement of alternative methods of collapse therapy, and disastrous results due to this is one of the causes of the fall in popularity of therapeutic pneumothorax.

In support of these statements I will show figures from three sources where I am responsible. In the Brompton clinic I exercise merely general supervision but the regular supervision and refills are done by a series of Chief Assistants and House Officers. In the Private and St. Bartholomew's Hospital Group I do all the work myself. In the Brompton group the patients have had their pneumothoraces instituted in many places and were taken on as they attended the clinic, i.e. many with pneumothoraces which in my opinion were unsatisfactory. In the other two series either the pneumothoraces were started by myself or I approved of their condition before taking them over. The series refers only to cases who were thought fit for discharge from the institutions where the pneumothoraces had been started, i.e. ambulant.

TABLE I

|                   | No. of<br>A.P.s | Empyemata | Empyemata<br>with<br>unclosed<br>cavities | Result                                    | Unclosed<br>cavities<br>without<br>empyemata | Result                                                    |
|-------------------|-----------------|-----------|-------------------------------------------|-------------------------------------------|----------------------------------------------|-----------------------------------------------------------|
| Brompton Clinic   | 217             | 44<br>20% | 18                                        | D.16<br>A. & W.<br>with $\theta$ 2<br>D.3 | 18                                           | D.16<br>A. & W.<br>with $\theta$ 2<br>D.3                 |
| St. Bart's Clinic | 61              | 3<br>5%   | 3                                         |                                           | 5                                            | A. & W.<br>with $\theta$ 2<br>D.3                         |
| Private Practice  | 45              | 5<br>11%  | 3                                         | A. & W. 1<br>A & W. .<br>with $\theta$ 2  | 3                                            | A. & W.<br>with $\theta$ 2<br>D. ( $\theta$<br>refused) 1 |

Empyemata are defined as having fluid which is turbid or thicker.  $\theta$  denotes thoracoplasty.

The figures show that in the Brompton series the percentage of empyemata (20%) is very high but much lower in the other series where selection was better and treatment carried out by one individual. The empyema cases with cavities and the cavity cases even without empyemata all died unless a thoracoplasty was performed with one exception in which the cavity was closed by the pressure of the increasing pus which was too thick to aspirate.

The early stages of the work on colitis were carried out as Will Edmunds Research Fellow (Royal College of Physicians).

## REFERENCES

- 1 RYLE, J. (1924) *Lancet* (ii), 101.
- 2 BOCKUS, H. L. (1944) *Gastro-Enterology*. Philadelphia, 2, 536.
- 3 — (1944) *Gastro-Enterology*. Philadelphia, 2, 538.
- 4 CULLINAN, E. R. (1938) *Brit. med. J.* (ii), 1351; WITTKOWER, E., *Brit. med. J.* (ii) 1356.
- 5 RUESCH, J. (1946) Chronic Disease and Psychological Invalidism. *Psychosomatic Medicine Monographs*, No. 9, New York.
- 6 GROEN, J. (1947) *Psychosom. Med.*, 9, 151.
- 7 DRURY, A. N., FLOREY, H., and FLOREY, M. E. (1929) *J. Physiol.*, 68, 173.
- 8 LIUM, R., and PORTER, J. (1939) *Arch. int. Med.*, 63, 210.
- 9 WOLF, S. G., and WOLFF, H. G. (1943) *Human Gastric Function*. London.
- 10 WHITE, B. V., Jr., and JONES, C. M. (1938) *New Eng. J. Med.*, 218, 191.
- 11 FRIEDMAN, M. H., and SNAPE, W. J. (1946) *Gastroenterology*, 7, 574.
- 12 ALMY, T. P., and TULIN, M. (1947) *Gastroenterology*, 8, 616.
- 13 CREDE, R. H., ROSENBAUM, M., and FEWIS, E. B. (1948) *Psychosom. Med.*, 10, 223.
- 14 SCHÜFFNER, W. A. P., and SNYDERS, E. P. (1928) *Verh. Ges. Verdaul. StoffwechselKr.*, 8, 135.
- 15 KOOLEMANS BEIJEN, G. J. W. (1928) *Verh. Ges. Verdaul. StoffwechselKr.*, 8, 148.
- 16 MACKIE, T. T., MILLER, D. K., and RHOADES, C. P. (1935) *Amer. J. trop. Med.*, 15, 571.
- 17 GOLDEN, R. (1941) *J. Amer. med. Ass.*, 117, 913.
- 18 RUFFIN, J. M., BAYLIN, G. J., and CAYER, D. (1945) *Gastroenterology*, 4, 289.
- 19 GLASS, W. H. (1948) *Amer. J. digest. Dis.*, 15, 297.
- 20 GOLDEN, R. (1941) *Radiology*, 36, 262.
- 21 KEKWICK, A. (1947) Personal communication.
- 22 FRAZER, A. C. (1946) *Physiol. Rev.*, 26, 103.
- 23 FABER, K. (1904) *Arch. VerdaulKr.*, 10, 333.
- 24 JUSTI, K. (1913) *Arch. Schiffs- u. Tropenhyg.*, 17, 505.
- 25 MANSON-BAHR, P. (1915) Report on researches on Sprue in Ceylon 1912-1914. London.
- 26 — (1924) *Lancet* (i), 1148.
- 27 MACKIE, F. P., and FAIRLEY, N. H. (1929) *Indian J. med. Res.*, 16, 799, 827.
- 28 THAYSEN, T. E. H. (1931) *Trans. R. Soc. trop. Med. Hyg.*, 24, 539.
- 29 — (1932) Non-tropical Sprue. London.

[January 25, 1949]

## DISCUSSION ON THE PLACE OF ARTIFICIAL PNEUMOTHORAX IN THE TREATMENT OF PULMONARY TUBERCULOSIS

Dr. F. H. Young (*Précis*): I find by reference to the *Proceedings of the Section*, 14, 15, that this subject was last discussed in 1921, twenty-seven years ago. There is still no general agreement (1) whether to use this method of treatment in individual cases, (2) how to handle details of treatment. It will, however, I think be generally agreed that apart from the potentiality of certain antibiotics, the selective collapse produced by the ideal pneumothorax is the most efficient method by which we can encourage the resistance of the patient to overcome the tuberculous process in his lungs, provided that all complications could be avoided. Since 1921, therapeutic pneumothorax has had a vogue which was certainly excessive, but lately the balance has swung the other way and some authorities seem to regard it as a dangerous proceeding which should only be used in exceptional cases. In my opinion this is a retrograde step. The trouble has been that the technique seems so easy that it is carried out by inexperienced workers who do not understand either the proper selection of cases or the finer points of its conduct.

It is now accepted that the following types are unsuitable for artificial pneumothorax even if possible: (a) Cases with dense fibrotic disease especially of the upper zones. In these a primary thoracoplasty is preferred provided that it is not otherwise contra-indicated. (b) Cases with active tracheobronchitis within the limits of bronchoscopic vision unless a subsequent pneumonectomy can be envisaged. Even if only a lobar bronchus is involved a subsequent spread may lead to permanent collapse of the whole lung. This also applies to the cases in which giant tension cavities are present which are undoubtedly produced by tracheobronchitis. Apart from these two types, if collapse therapy is indicated, a trial pneumothorax would be considered in all cases where the respiratory reserve is sufficient if all complications, especially pleural, could be avoided.

The main complications are threefold: (1) the occurrence of tuberculous empyema with or without a bronchopleural fistula; (2) bronchogenic spreads of disease mainly to the other

due to physical strain, anxiety, minor ailments, pregnancies, change in diet and other factors not encountered during the recovery period at the sanatorium. It is of primary importance that the physician treating the patient should be acquainted with all relevant details of the case immediately after the discharge from the sanatorium.

*The Problem of X-ray information.*—Many physicians are of the opinion that reports on skiagrams are insufficient and that the films themselves should be sent along with the clinical notes. Here we come up against a real problem for many physician-superintendents are reluctant to part with X-ray films and have not the means to make reductions or the inclination to duplicate even the important films of a series. The only solution is, either to have a duplicate set of X-ray films, which would be both expensive and impracticable, or a system by which reductions are made of all important skiagrams. These should then accompany the clinical records wherever they may be sent. Paper films have been used for this purpose but they are not popular as they are sometimes difficult to read and do not always present the finer details very clearly.

Some time ago I approached a leading industrial firm with a view to establishing a service that would enable hospitals, clinics and sanatoria to obtain reductions of all important skiagrams on a weekly collecting and distributing scheme. The only obstacle was the cost, but I was told that if the numbers were large enough there was no reason why this difficulty should not be overcome. There is a vast field of work to be explored by an enterprising firm, or by employing the disabled, in establishing such a service which would not only create a successful industry but would meet a need that is retarding progress in all parts of the country.

*Aids to patients.*—It is helpful if patients can continue treatment without having to obtain leave of absence from work as this not only may mean loss of income but will advertise their disability. They should not be put to any expense in attending for refills and authority for payment of travelling expenses should rest with the physician. Waiting time at the clinic should be reduced to a minimum by a system of regular appointments. In the case of married women due recognition must be given to her household duties and responsibilities when fixing the date and time for refills. These points are usually met quite easily in urban districts but in many rural areas long distances have to be travelled by patients from their homes to the chest clinics. If there is no X-ray plant at the chest clinic this adds further complications of transport and fixing appointments for the skiagrams or screening which are essential for good treatment. In some centres refills are given without previous radiographic examination, a film or screening every two or three months being thought sufficient. This practice can cause serious complications to arise. Surely pneumothorax treatment in out-patients should be administered with care and with controls equal to or even greater than in the case of in-patients. If the number of patients is too large for the clinic staff to provide this care then the staff should be increased and not attempt to cope with larger numbers of patients with the same staff by decreasing the degree of control.

*Bed patients.*—The bedridden patient requiring pneumothorax refills presents a number of further problems. With the shortage of available beds there should be a tendency to send home, where possible, the chronic case that is making no progress. Care should be taken that collapse therapy in these cases is not continued unnecessarily. Relapses during domiciliary treatment necessitating ambulance transport for refills at the chest clinic or home attendance by the physician are sometimes due to treatment being incomplete when the patient is discharged from the sanatorium. Particular care is needed in cases with bilateral pneumothorax. These patients so often do well under sanatorium conditions but relapse under domiciliary treatment. This is no fault of the physician at the clinic but owing to an unstable clinical condition and poor resistance the patient is unable to stand the strain and anxiety of domiciliary environment.

The termination of the pneumothorax treatment can also bring its difficulties if such conditions are present as residual bronchiectasis or uncollapsed cavities, or the complications which follow the unrelieved tension set up by a rigid mediastinum and a dense obliterative pleuritis.

Minor complications, mainly connected with pleural effusions, may occur, and may require admission for one or two nights to a hospital or sanatorium. There should, therefore, be an arrangement by which these beds can be easily obtained and, if possible, the physician of the clinic should be intimately associated with the treatment of these patients in the institution.

How long refills should be maintained after discharge from sanatorium depends very largely on the condition of the lung prior to the induction of the pneumothorax. For this reason it is of great importance that the original skiagrams, or satisfactory substitutes, taken before the induction are available for the physician of the chest clinic. Many cases terminate spontaneously although somewhat prematurely, in others some decision must be made.



TABLE II  
Total No. of No. of empyema  
empyemata without cavities % of A.P.s Results

|                                 |    |    |    |    |     |                                |
|---------------------------------|----|----|----|----|-----|--------------------------------|
| Brompton Clinic                 | .. | .. | 44 | 26 | 14% | A & W. 20<br>D. 6 <sup>1</sup> |
| Private Practice and St. Bart's |    |    | 8  | 2  | 4%  | A. & W. 2                      |

<sup>1</sup>4 died from spreading disease in the other lung.

Where fluid or even pus appears in the pleural cavity danger to life is not considerable unless there is an underlying cavity. The figures for these are usually published by surgeons to whom only the cases unsuccessfully treated by physicians are submitted. The occurrence of empyemata without unclosed cavities is much higher in the first group. I feel that this is due to continuous treatment by one individual.

TABLE III.—(PRIVATE CASES)

| No. of A.P.s in cases who are alive | Little or no apparent lack of function | Loss of function less than $\theta$ | Loss of function equivalent to $\theta$ | Worse than $\theta$ |
|-------------------------------------|----------------------------------------|-------------------------------------|-----------------------------------------|---------------------|
| 43                                  | 25<br>58%                              | 8<br>19%                            | 8<br>19%                                | 2<br>4%             |

The problem of the loss of function which occurs as a final result of a therapeutic pneumothorax is less susceptible of control, prophecy prior to the final result, and even accurate assessment.

These figures are very approximate but they show that the claim that a primary thoracoplasty should be preferred to an artificial pneumothorax, where possible, is hardly tenable, at any rate where full personal treatment is possible.

The Brompton series had a much higher percentage of unclosed cavity cases so in the

TABLE IV.—RESULTS

|                      | Total No. of patients | Total No. of A.P.s | Decd. or dying | A. & W.    | A. & W. (unclosed cavities excluded) |
|----------------------|-----------------------|--------------------|----------------|------------|--------------------------------------|
| Brompton             | 204                   | 217                | 66<br>32%      | 138<br>68% | 80%                                  |
| St. Bart's           | 57                    | 62                 | 8<br>14%       | 49<br>86%  | 96%                                  |
| Private Practice     | 42                    | 46                 | 3              | 39<br>93%  | 93%                                  |
| St. Bart's + Private | 99                    | 108                | 11<br>11%      | 88<br>89%  | 95%                                  |

last column I omitted these. However, the difference in results persists and I believe that the most important cause of failure is lack of continuity of treatment. The best results will be obtained in cases where the whole of the treatment is carried out by an individual, so much so that in the decision whether a therapeutic pneumothorax should be tried and, if tried, kept up, the question whether the treatment will be carried out continuously by one individual should play a prominent part.

In conclusion I feel that the revulsion against trial (and I must emphasize the word) therapeutic pneumothorax has gone too far, and if cases are correctly chosen and treatment carried out in the way I have indicated, while continuity of treatment is obtained, the results are good.

Dr. F. R. G. Heaf: *The post-sanatorium care of A.P. cases. Change from sanatorium to domiciliary environment.*—It is not always realized how great is the change between the quiet orderly routine of sanatorium life and the irregular rush of work and play in the average household to which a patient returns on completion of institutional treatment. Although the patient appears to have stabilized himself under sanatorium conditions we cannot be sure that there are no residual foci of active disease, neither have we any knowledge how the patient's resistance will be maintained under domiciliary conditions. After his discharge there will be considerable fluctuations in the specific resistance to tuberculosis

## Section of Odontology

President—Professor SHELDON FRIEL, M.Dent.Sc., Sc.D., F.D.S.

[January 10, 1949]

### Dental Caries in Norwegian Children During and After the Last World War. A Preliminary Report

By GUTTORM TOVERUD, Ph.D.

(*Professor of Pedodontia, The Dental School of Norway, Oslo.*)

**ABSTRACT.**—A preliminary report is submitted on the occurrence of dental caries in Norwegian children, during and after the World War.

Dental examinations of 8,000 to 9,000 school children from different parts of Norway have been carried out each year from 1940 to 1948. It is concluded from the statistical results of the investigation that the caries frequency decreased steadily from year to year during the war. The reduction in the number of carious tooth surfaces per child from the beginning of the war to the lowest number some time after the war ended amounts to 50 to 75%.

A study has also been undertaken on 600 to 700 children, 2½ to 7 years old. The results in this younger group show even a greater reduction.

In both groups the decrease is statistically significant.

From 1946 the caries frequency has increased again in the school children as well as in the pre-school children. In both groups the increase is statistically significant.

The turn of the caries curve after the war differs according to the age-group.

The cause of the decrease in caries frequency during the war and the cause of the increase after the war is discussed. Based on the rationing of the various food articles our tentative conclusion is that the decrease may be attributed to the lowering in consumption of refined carbohydrates and the increase in consumption of more natural foods, i.e. protective foods. This may have resulted in an increased resistance of the teeth and a reduction in the local factors which produce decay.

More detailed studies of the change in caries frequency as well as of the change in food consumption and habit of living during and after the war are necessary before a definite conclusion can be drawn. Such studies are being continued.

DURING and after the first world war a distinct reduction in caries frequency in school children was observed in Norway as well as in other countries touched by the war in some way, Ramm (Norway), Bensow (Sweden), Wheatley (England), Wimmenauer (Germany). These facts, though of great interest, were not given due attention at that time.

When the war broke out in September 1939 the Pedodontic Department of the Dental School of Norway planned a comprehensive study of the caries frequency among pre-school and school children during the war period. The study of the school children was planned in collaboration with the school dentists.

Detailed knowledge of the patient's condition and the state of the expanding lung call for more, rather than less, frequent examinations when artificial pneumothorax treatment is being terminated.

I should like to say a word about the induction of "protective A.P.s" whilst the patient is at home awaiting a bed at a sanatorium. This treatment is not one of choice. Nobody would attempt it if it were not for the bed situation, owing to the great risks involved. Much depends on the judgment of the physician and his personality, but one thing is essential, that is a good ambulance service to enable the patient to receive adequate radiographic control. Without this service the treatment should not be attempted.

*Need for statistics on the results of A.P.T.*—Finally I would make a plea for keeping full records and clinical notes of the patient's condition and the development of a system by which the after-history of the patient may be followed for five or even ten years. Our knowledge of the after-histories of pneumothorax cases is very incomplete. Little has been done since the report of F. R. Bentley which was published by the Medical Research Council in 1938. There are some who now consider that treatment by major surgery, as an initial measure, is preferable to artificial pneumothorax. We are still not sure to what extent artificial pneumothorax treatment has improved the expectancy of life of tuberculous persons. We cannot say for certain how much permanent benefit can be expected from the treatment. Such important knowledge can only be obtained by keeping careful records preferably on a standardized coded card that can be used in conjunction with the modern machines now being installed in statistical departments. The work will have to be planned and carried out by teams working in the larger centres, and as the results will not be available for a number of years the groundwork should be commenced at the earliest possible moment.

Dr. Philip Ellman, whose paper, with illustrations, will be published *in extenso* in the *Post-Graduate Medical Journal*, May, 1949, dealt at length with the main difficulties and disadvantages experienced in pneumothorax therapy. He pointed out that the efficiency of results corresponded to the quality of the pneumothorax and said that the poorer the initial pneumothorax, the more unfavourable was the pneumothorax life and the permanent result. He outlined the indications for pneumothorax treatment, and deprecated strongly the employment of the so-called "crash-pneumothorax" in the early stages of the disease. He then discussed the mechanics of cavity closure and the importance of tracheo-bronchial tuberculosis in relation to it, pointing out that tracheo-bronchial disease, which often led to broncho-stenosis, was a contra-indication to the induction of a pneumothorax. After mentioning some of the chief complications liable to arise during pneumothorax therapy, he concluded by reminding his audience that pulmonary tuberculosis was primarily a general constitutional disease which, together with the mechanical state of the bronchi, influence the response of the local (lung) lesion to treatment.

Tables I and II show the average caries-affected teeth per child in different years in tooth-age groups 12 and 28. The reduction from 1940-41 to 1945-46 amounts to 36% in the youngest group and to 32% in the oldest group.

The decrease in the total amount of caries will be far clearer when we calculate according to caries-affected *surfaces* instead of teeth. Unfortunately the material as a whole has not yet been worked out on the basis of tooth surfaces. However, by the courtesy of E. Alexander, a school dental surgeon, I am able to demonstrate such figures from his particular district, Gjerpen, Table III.

TABLE III.

THE SCHOOL DENTAL CLINIC OF GJERPEN (ALEXANDER). NUMBER OF CARIOUS SURFACES PER CHILD

| Year                    | 1939-40 | 40-41 | 41-42 | 42-43 | 43-44 | 44-45 | 45-46 | 46-47 | 47-48 |
|-------------------------|---------|-------|-------|-------|-------|-------|-------|-------|-------|
| 1st grade (7-8 years)   |         |       |       |       |       |       |       |       |       |
| No. of car. surf. ..    | 3.9     | 3.0   | 2.3   | 1.4   | 0.9   | 0.8   | 0.6   | 0.6   | 1.2   |
| 7th grade (13-14 years) |         |       |       |       |       |       |       |       |       |
| No. of car. surf. ..    | 19.3    | 21.8  | 20.1  | 17.8  | 14.2  | 12.7  | 10.9  | 8.0   | 6.6   |

In each grade approx. 130 children per year.

Table III shows that the number of caries-affected surfaces per child by children in the first grade (7-8 years old) has decreased from 3.9 in 1939-40 to 0.6 in 1945-46. This reduction amounts to 82%. In children in the 7th grade (approximately 13-14 years old) the number of carious surfaces per child has decreased from 19.3 in 1939-40 to 10.9 in 1945-46, a reduction of 44%. However, it will be seen from the table that the number of caries attacks in this grade is becoming less. By figuring out the reduction from 1939-40 to 1947-48 we find this to be 66%.

As far as may be seen from the preliminary data, the average decrease in the number of caries-affected tooth surfaces in Norwegian school children during the war amounts to 50 to 75%.

#### RESULTS OF DENTAL EXAMINATION OF PRE-SCHOOL CHILDREN

The number of pre-school children examined has not been as large as that of the school children. Three small communities 15-30 miles outside Oslo were chosen for our main survey. 600 to 700 children from 2½ to 7 years old have been examined in the years 1939, 1944, 1945, 1946, 1947 and 1948. In one of the communities the dental examination has been carried on from 1936. Only a few examples of the change in caries frequency will be demonstrated.

To illustrate the change in caries frequency during the war the mean value of the caries figures of 1944 and 1945 are compared with the mean value of the caries figures of 1936-40. Both groups consist of about the same number of children, 1,142 and 1,120 respectively. As will be seen from fig. 3 the decrease in the percentage of caries-affected teeth is very marked in children between 2½ and 7 years of age. The decrease is highest in the six anterior teeth in the lower jaw and amounts to about 80% compared with 30 to 50% for the molars. Thus it is evident that the change in caries-frequency in the temporary teeth is about the same as that in the permanent teeth.

In an analysis of the caries rate of the different tooth surfaces during the same periods it was seen that occlusal caries had not decreased as much as had caries on the smooth surfaces. This is also what would be expected as fissure caries is the most common type of caries. The percentage reduction of occlusal caries is about 40-45 and that of the smooth surfaces about 60-75.

Fig. 4 demonstrates the difference in the caries picture according to the age of the children. From two of the three rural communities we have taken out the age-groups: 2½-3 years, 4-5 years and 6-7 years. As will be seen from the age-group 2½-3 years we find almost the same percentage decrease in caries-affected children as in caries-affected teeth and in caries-affected surfaces. From the age-group 4-5 years it is seen that the decrease in percentage of caries-affected children is much less than the decrease in D.M.F. teeth and this again is less than the decrease in carious surfaces. Looking at the age-group 6-7 years, it is seen that the decrease in caries-affected children is not noticeable till 1947 and even in this year to a slight degree.

As mentioned before, the caries frequency in the permanent teeth is increasing since the war. The same is also true in the temporary teeth. This is clearly illustrated in fig. 5 from one of the rural communities, Skedsmo. In the three youngest age-groups we find that the curves turn upwards from the year 1945. In the age-group 5-6 this change takes place in

It was our intention to obtain a fair representation of school children in the age-group 7 to 14 years from the various parts of Norway. Unfortunately, soon after the plan had been put into practice, Norway was invaded by the Germans, and as a consequence, many difficulties arose. Therefore, we have not been able to get exact dental records of more than from 8,000 to 9,000 children for each of the years 1940 to 1948.<sup>1</sup>

# RESULTS OF DENTAL EXAMINATION OF SCHOOL CHILDREN

Fig. 1, which includes boys of tooth-age 12 (having the 8 permanent incisors and the 4 first permanent molars), demonstrates two interesting facts. A considerable difference is seen in the number of caries-free boys (not counting the temporary teeth) in the three groups: The lowest percentage occurs in towns and the highest in rural districts. It is most striking that the percentage of caries-free children in all three groups has increased considerably during the war. In towns the increase is from near zero when the war broke out in Norway to above 20% in the first post-war year.

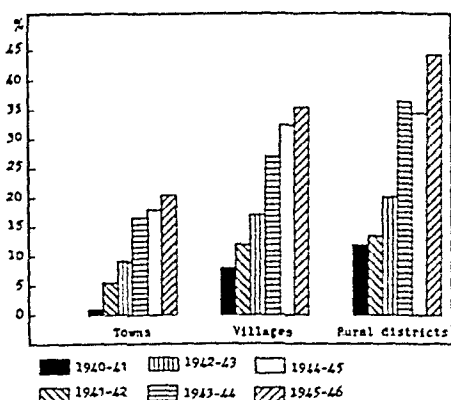


FIG. 1.—Percentage of boys with caries-free permanent teeth, tooth-age 12.

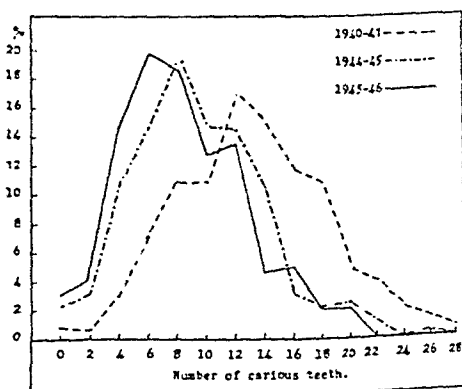


FIG. 2.—Distribution of boys according to number of carious teeth. Village boys of tooth-age 28.

The changes in the caries distribution is evident from the curves in fig. 2, which comprises village boys of tooth-age 28 and shows the percentage distribution of children according to the number of teeth affected. In order to get a clearer view, the years 1941, 1942, 1943 and 1944 are omitted. In 1940-41 the peak of the curve is represented by the group having 12 carious teeth each. In 1944-45, on the other hand, the group having only 8 carious teeth is on the highest point of the curve. During the first post-war year the change is even greater with the peak in the "6 carious teeth" group, so that the highest percentage group has moved from the group of 12 carious teeth down to the group of 6 carious teeth.

Thus the peak of the curve has been displaced towards zero. 0.6% of the children showed 28 carious teeth in 1940-41 while during the year 1945-46 nobody had a greater number of caries-affected teeth than 22.

TABLE I.  
AVERAGE CARIES-AFFECTED TEETH PER CHILD DURING DIFFERENT YEARS.  
VILLAGE CHILDREN OF TOOTH-AGE 12\*

| Year                 | 1940-41 | 41-42 | 42-43 | 43-44 | 44-45 | 45-46 |
|----------------------|---------|-------|-------|-------|-------|-------|
| No. of car. teeth .. | 3.64    | 3.57  | 3.48  | 2.86  | 2.60  | 2.33  |

TABLE II.  
AVERAGE CARIES-AFFECTED TEETH PER CHILD DURING DIFFERENT YEARS.  
VILLAGE CHILDREN OF TOOTH-AGE 28\*

| Year                 | 1940-41 | 41-42 | 42-43 | 43-44 | 44-45 | 45-46 |
|----------------------|---------|-------|-------|-------|-------|-------|
| No. of car. teeth .. | 13.3    | 13.2  | 12.0  | 10.6  | 9.8   | 9.1   |

\*The phrase "tooth-age" is understood to mean the number of erupted permanent teeth.

<sup>1</sup>Besides this study conducted by the Pedodontic Department several reports have appeared from different school dental clinics in Norway. During the first two years all the teeth were examined but later only the teeth on the right side.

1946 and in the oldest group in 1947. Fig. 5 must be explained. The three lowest curves dropped before the war much more than the curves for the two older age-groups. The explanation for this difference is that children up to the age of 5 years have attended a health station erected for mothers and children in 1936. This health work has decreased the caries rate of the children to a considerable extent.

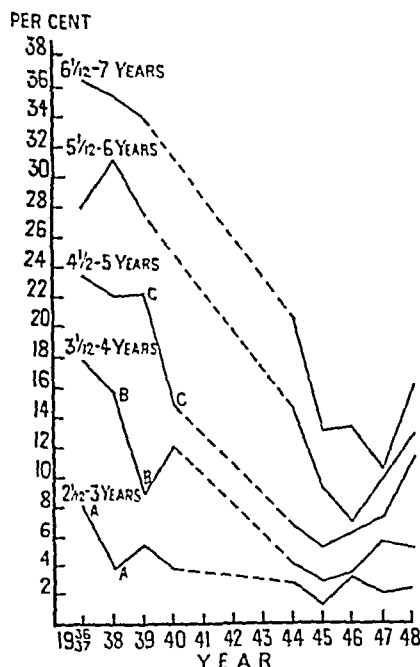


FIG. 5.—Showing the decrease during the war in percentage DMF surfaces in temporary teeth of children up to the age of 7 years.

The difference in figures from pre-war to the lowest value after the war has been statistically analysed. This analysis shows that the decrease in all age-groups is significant (see Table IV). The increase in caries frequency from the lowest values after the war up to 1948 is analysed in the same manner. Here, too, it can be seen that the difference is significant (see Table V).

TABLE IV.

| DECREASE IN DECAYED, MISSING AND FILLED TEETH PER CHILD |      |           |     |      |            |                                     |
|---------------------------------------------------------|------|-----------|-----|------|------------|-------------------------------------|
| Age-group                                               | Year | DMF teeth |     | Year | Difference | Difference<br>Stand. error of diff. |
|                                                         |      | No.       | No. |      |            |                                     |
| 2½-3                                                    | 1939 | 2.4       |     | 1945 | 0.9        | 2.73                                |
| 3-4                                                     | 1939 | 6.5       |     | 1945 | 2.1        | 7.96                                |
| 4-5                                                     | 1939 | 9.5       |     | 1945 | 3.6        | 10.05                               |
| 5-6                                                     | 1939 | 10.9      |     | 1946 | 4.8        | 11.49                               |
| 6-7                                                     | 1939 | 11.5      |     | 1947 | 5.4        | 8.74                                |

TABLE V.

| INCREASE IN DECAYED, MISSING AND FILLED TEETH PER CHILD |      |           |     |      |            |                                     |
|---------------------------------------------------------|------|-----------|-----|------|------------|-------------------------------------|
| Age-group                                               | Year | DMF teeth |     | Year | Difference | Difference<br>Stand. error of diff. |
|                                                         |      | No.       | No. |      |            |                                     |
| 2½-3                                                    | 1945 | 0.9       |     | 1948 | 1.8        | 2.51                                |
| 3-4                                                     | 1945 | 2.1       |     | 1948 | 3.6        | 3.55                                |
| 4-5                                                     | 1945 | 3.6       |     | 1948 | 5.7        | 4.12                                |
| 5-6                                                     | 1946 | 4.8       |     | 1948 | 6.2        | 2.32                                |
| 6-7                                                     | 1947 | 5.4       |     | 1948 | 7.1        | 3.21                                |

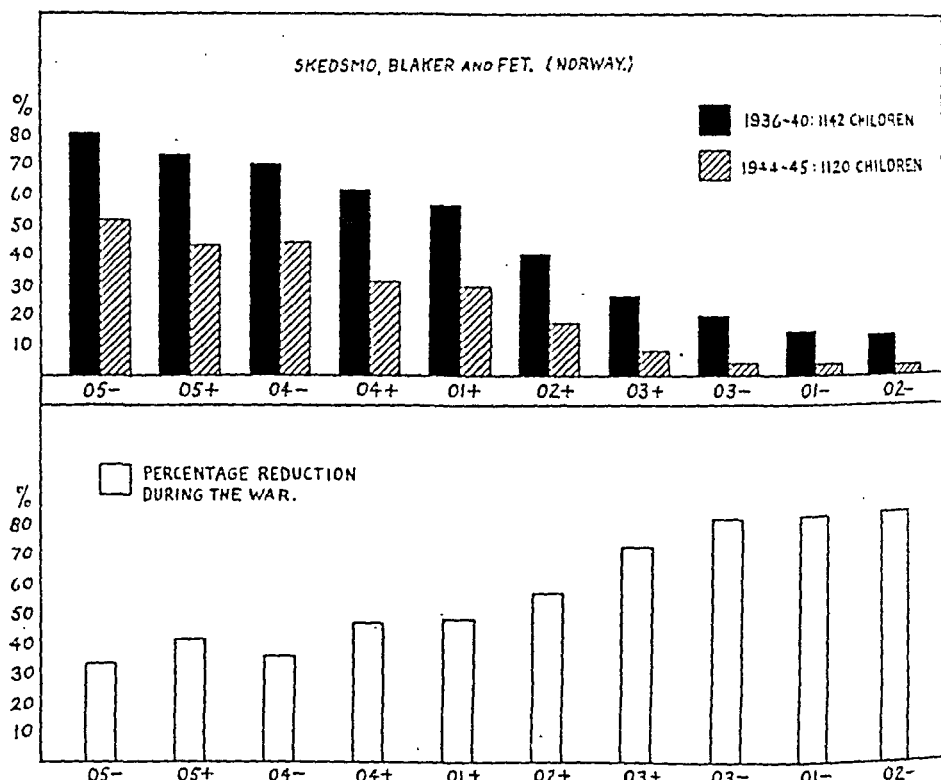


FIG. 3.—Percentage of DMF teeth (upper chart) and percentage reduction during the war in the different morphological types of deciduous teeth of children 2½ to 7 years (Sinde).

### BLAKER AND FET.

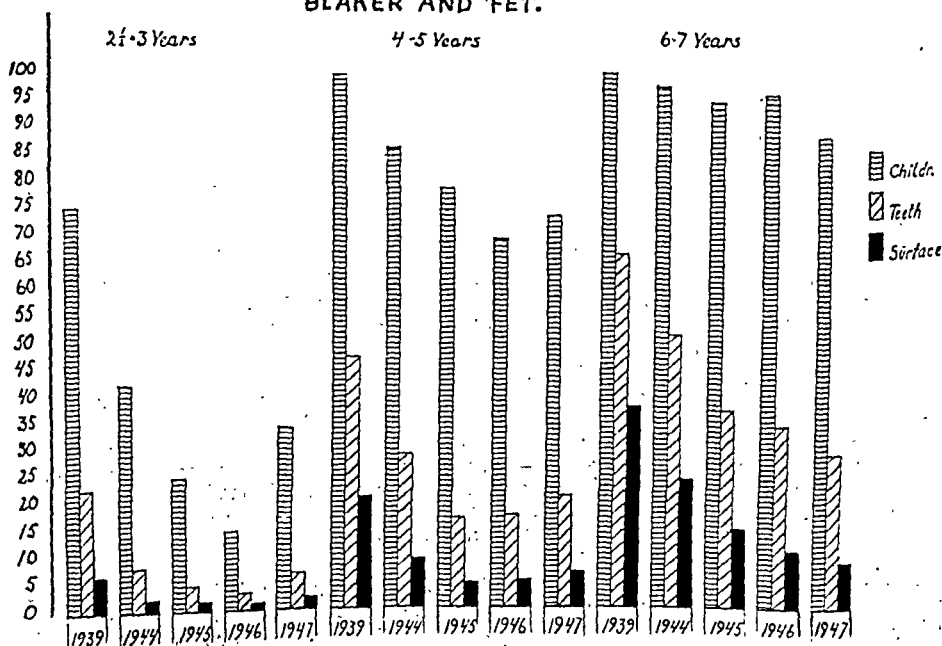


FIG. 4.—Percentage of children, teeth and tooth surfaces showing caries.

the relatively high intake of minerals and vitamins A and D. The children of pre-school age did not show any deviation in height and weight from those in previous years. The protective food for the school children, however, was not so good as before the war. These children also showed a lower height and weight curve in the late years of war than previously, with increased morbidity, except for caries.

As has been stated before, the rationing of the protective foods was such as to meet as far as possible the need of the pregnant and nursing mother and the child up to 6 years of age. It is also true generally that the intake of protective food in these groups was more regular and abundant than before the war. Much of the refined carbohydrates used before the war was substituted by more natural food. In this connexion it is of interest to remember the important experiments on rats made by Sognnaes. He found that the susceptibility to dental caries is greater the earlier in the rat's life the high sugar diet is given, either to the rat itself or to the mother. The highest caries score in the young rat was found when the mother was put on the 67% sucrose diet even before the gestation.

Do we find in our material any correspondence between the mineralization of the teeth during the rationing period and the decrease in caries rate? The following tables will give the answer. By studying Table VIII we find the mineralized teeth of 7-year-old school children, the percentage of teeth with pre-eruptive mineralization, and the lowest number of carious surfaces

RAJASTHAN DISPENSARY, RJP No 146-6000 00  
RAJASTHAN MEDICAL DEPARTMENT  
( Out-Patient Ticket )  
Hospital/Dispensary  
195

No. \_\_\_\_\_ Dated \_\_\_\_\_  
Name \_\_\_\_\_ Sex \_\_\_\_\_  
Age \_\_\_\_\_ Caste \_\_\_\_\_  
Disease \_\_\_\_\_

| PERMANENT TEETH.             |                    |
|------------------------------|--------------------|
| Years of pre-erupt. mineral. |                    |
| Treatment                    | 1931-32 to 1936-37 |
|                              | 1932-33 to 1937-38 |
|                              | 1933-34 to 1938-39 |
|                              | 1934-35 to 1939-40 |
|                              | 1935-36 to 1940-41 |
|                              | 1936-37 to 1941-42 |
|                              | 1937-38 to 1942-43 |
|                              | 1938-39 to 1943-44 |
|                              | 1939-40 to 1944-45 |
|                              |                    |
| Date                         | 1931-35            |
|                              | 1936-40            |
|                              | 1937-41            |
|                              | 1938-42            |
|                              | 1939-43            |
|                              | 1940-44            |
|                              |                    |
|                              |                    |
|                              |                    |
|                              |                    |

year broke out. But the figure has mineralized in a still better period. resistance is not only dependent of varying factors during the post-eruptive period. It is not possible to ascribe the decrease in caries rate to the rationing, showing the condition of the

TEMPORARY TEETH  
pre-erupt. mineral.

TABLE VIII.

| 3-YEAR-OLD CHILDREN (FROM PERMANENT AND TEMPORARY) |                                           |
|----------------------------------------------------|-------------------------------------------|
| Year of exam.                                      | Percentage of pre-eruptive mineralization |
| 1939                                               | 193                                       |
| 1944                                               | 193                                       |
| 1945                                               | 940                                       |
| 1946                                               |                                           |
| 1947                                               |                                           |
| 1948                                               |                                           |

in caries rate. But the teeth were mineralized before



The statistical analysis has been performed by my assistant dental surgeon, Mr. O. E. Sunde, according to the following principles:

| AGE-GROUP 21-3 YEARS. SKIDSVÅG, BLAKER AND VET |                 |                  |                               |                                                           |                                 |                                                              |                          |                                                |
|------------------------------------------------|-----------------|------------------|-------------------------------|-----------------------------------------------------------|---------------------------------|--------------------------------------------------------------|--------------------------|------------------------------------------------|
| Year                                           | a<br>No. of ch. | b<br>S DMF teeth | c<br>Mean DMF teeth pr. child | d<br>(Mean DMF teeth) <sup>2</sup><br>(= c <sup>2</sup> ) | e<br>S (DMF teeth) <sup>2</sup> | f<br>S (DMF teeth) <sup>2</sup><br>÷ No. of ch.<br>(= e ÷ a) | g<br>Difference<br>f - d | h<br>Standard deviation<br>$\sigma = \sqrt{g}$ |
| 1939                                           | 44              | 108              | 2.45                          | 6.00                                                      | 776                             | 17.64                                                        | 11.64                    | 3.42                                           |
| 1945                                           | 89              | 82               | 0.92                          | 0.84                                                      | 472                             | 5.30                                                         | 4.46                     | 2.11                                           |

$$\epsilon \text{ diff} = \sqrt{\frac{\sigma_1^2}{n_1} + \frac{\sigma_2^2}{n_2}} = \sqrt{0.3146} = 0.56 (= \text{the standard error of the difference})$$

$$\text{Difference mean}_1 - \text{mean}_2 = 2.45 \text{ DMF teeth} - 0.92 \text{ DMF teeth} = 1.53$$

$$\text{Difference} \div \epsilon \text{ diff} = 1.53 \div 0.56 = 2.73$$

When the difference between the mean decayed, missing and filled teeth amounts to 2.5 (or 2.0) times its standard error it is a significant one.

(The standard deviation and the standard error of the difference have been calculated according to Bradford Hill: Principles of Medical Statistics.)

### FOOD AND MODE OF LIFE IN NORWAY DURING THE WAR

Nearly all food articles were rationed. Milk: Pregnant and nursing women, and children up to 6 years of age, were allowed 0.75 litre per day. It was not always possible to get that amount; however, it is believed that the children mostly did, as the mothers were very anxious to give it to them. Children from 6 to 16 years of age were allowed only 0.5 litre per day. Teen-ages from 16-18 were allowed 0.25 litre of whole milk and 0.25 litre of skimmed milk. Adults had just 0.25 litre of skimmed milk.

*Cod-liver oil.*—Preference was given to pregnant and nursing women and pre-school children. School children also had access to cod-liver oil but not as regularly as the groups mentioned. *Cheese* was very scarce and indeed non-existent for several months. There was no cream. The *margarine* ration was very low: 30 grammes per day including some butter now and then. *Meat* and *pork* were rarely obtainable on coupons. *Fresh fish* was difficult to obtain, whereas herring and salted and dried fish were more plentiful. The consumption of *potatoes* was greater than usual. *Vegetables*, particularly turnips and carrots, were also more in use than in previous years. The *bread ration* was far too small for growth and for heavy work. The flour was of 95% extraction and 0.4% calcium-carbonate was added from the end of 1942. A whiter bread was given only on a medical prescription. The bread was not allowed to be sold before it was twenty-four hours old.

The *sugar ration* was about 30 grammes per day from 1940 and throughout the whole war period. Some sugar was allowed for canning, and by adding this, the whole sugar ration amounted to about 37 grammes per day as an average. The sugar ration to bakers and industrial concerns was constantly lowered during the war, so that the ration in 1944 just amounted to a quarter of what was used in 1939 for bakers and to one-eighth for industry. The result was that sugared cakes, chocolate, candy, and marmalade disappeared from the market. During the last two to three years of war, candy was not available at all.

*Coffee* and *tea* were substituted by home products.

If we compare the food during the war with the previous years, it is found that the average daily consumption of whole milk, meat, fat, fresh fish, bread and flour, fruit, sugar and sugar-products, coffee and tea was much lowered, the daily calorie-intake, too, was lowered. The milk producers, however, used as an average more milk and butter than usual. The same is probably true of meat and fat.

### POSSIBLE CAUSES OF DECREASE IN CARIES FREQUENCY

This question is of the greatest scientific as well as practical interest. If it were possible to come to a positive conclusion, it would be a step nearer the solution of the aetiology of caries and provide a sound basis for prophylaxis.

Two main factors must be considered, i.e. the resistance of the tooth and the direct caries-producing agencies.

### THE RESISTANCE OF THE TOOTH: TOOTH MINERALIZATION

Increased resistance must depend on better nutrition as far as mineralization is concerned.

According to the allowances for pregnant and nursing mothers, and children up to 6 years of age, the mineralization of the teeth in the pre-eruptive period should be satisfactory by

the relatively high intake of minerals and vitamins A and D. The children of pre-school age did not show any deviation in height and weight from those in previous years. The protective food for the school children, however, was not so good as before the war. These children also showed a lower height and weight curve in the late years of war than previously, with increased morbidity, except for caries.

As has been stated before, the rationing of the protective foods was such as to meet as far as possible the need of the pregnant and nursing mother and the child up to 6 years of age. It is also true generally that the intake of protective food in these groups was more regular and abundant than before the war. Much of the refined carbohydrates used before the war was substituted by more natural food. In this connexion it is of interest to remember the important experiments on rats made by Sognnaes. He found that the susceptibility to dental caries is greater the earlier in the rat's life the high sugar diet is given, either to the rat itself or to the mother. The highest caries score in the young rat was found when the mother was put on the 67% sucrose diet even before the gestation.

Do we find in our material any correspondence between the mineralization of the teeth during the rationing period and the decrease in caries rate? The following tables will give the answer. By studying Table VI, i.e. the permanent teeth of 7-year-old school children, we find the lowering of the number of carious surfaces of teeth with pre-eruptive mineralization long before the war. It is true, though, that the lowest number of carious surfaces

TABLE VI.  
7-YEAR-OLD CHILDREN FROM GJERPEN. PERMANENT TEETH.  
(ALEXANDER)

| Year of exam. | No. car. surf. per child | Years of pre-erupt. mineral. |
|---------------|--------------------------|------------------------------|
| 1939-40       | 3.9                      | 1931-32 to 1936-37           |
| 1940-41       | 3.0                      | 1932-33 to 1937-38           |
| 1941-42       | 2.3                      | 1933-34 to 1938-39           |
| 1942-43       | 1.4                      | 1934-35 to 1939-40           |
| 1943-44       | 0.9                      | 1935-36 to 1940-41           |
| 1944-45       | 0.8                      | 1936-37 to 1941-42           |
| 1945-46       | 0.6                      | 1937-38 to 1942-43           |
| 1946-47       | 0.6                      | 1938-39 to 1943-44           |
| 1947-48       | 1.2                      | 1939-40 to 1944-45           |

corresponds to a mineralization period partly after the war broke out. But the figure has doubled during the year after, and these teeth have been mineralized in a still better period.

As has been stressed, particularly by May Mellanby, the resistance is not only dependent on the pre-eruptive mineralization, but also on the calcifying factors during the post-eruptive period. But not even by taking this into account is it possible to ascribe the decrease wholly to an increased resistance of the teeth. Table VII showing the condition of the temporary teeth of 6-year-old children demonstrates the same.

TABLE VII.  
6-YEAR-OLD CHILDREN (FROM BLAKER AND FET). TEMPORARY TEETH

| Year of exam. | Per cent car. surf. | Years of pre-erupt. mineral. |
|---------------|---------------------|------------------------------|
| 1939          | 38                  | 1931-35                      |
| 1944          | 25                  | 1936-40                      |
| 1945          | 15                  | 1937-41                      |
| 1946          | 11                  | 1938-42                      |
| 1947          | 9                   | 1939-43                      |
| 1948          | 14                  | 1940-44                      |

To a certain degree Table VIII, comprising children of the age-group 3-4 years, may be taken as an expression of the view that a difference in resistance alone is responsible for the change

TABLE VIII.  
3-YEAR-OLD CHILDREN (FROM BLAKER AND FET)

| Year of exam. | Per cent car. surf. | Years of pre-erupt. mineral. |
|---------------|---------------------|------------------------------|
| 1939          | 15                  | 1934-38                      |
| 1944          | 5                   | 1939-43                      |
| 1945          | 3                   | 1940-44                      |
| 1946          | 4                   | 1941-45                      |
| 1947          | 3                   | 1942-46                      |
| 1948          | 5                   | 1943-47                      |

in caries rate. But even here we might have found, if examined, the first decrease in teeth mineralized before the rationing actually was stabilized.

*Thus it cannot be stated that the change in caries frequency during and after the war is solely dependent on a change in tooth resistance.*

#### DIRECT CARIES-PRODUCING AGENCIES

These are the bacteria and the refined carbohydrates. Unfortunately we have not made any comparative study of the oral bacterial flora during the war. The intake of refined carbohydrates, however, has been much less during the war than before. As has been stated and proved over and over again by many investigators (Jay, 1947), a positive correlation exists, as a rule, between the amount of ingested refined carbohydrates, especially of sugar and the acid-producing bacteria in the mouth. When the intake of sugar and all kinds of sweets was reduced considerably, one may also suppose a change in the bacterial flora.

The curves in fig. 6 demonstrate the total consumption of sugar, the daily ration plus the extra amount for canning and other purposes, the quota for industry and for bakeries.

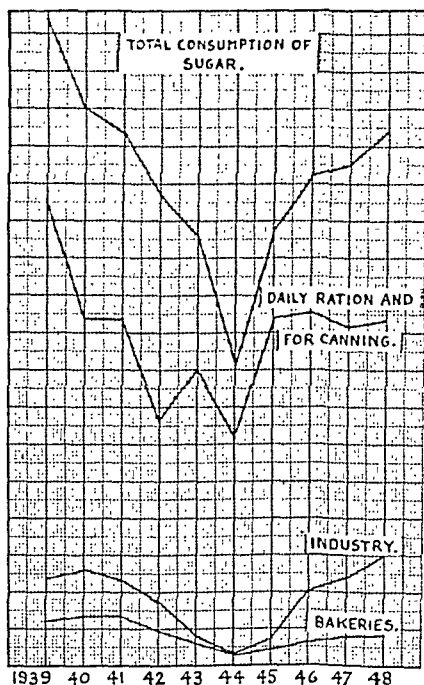


FIG. 6.—Graph showing consumption of sugar.

All 4 curves are drawn in the right proportion to each other. (The exact figures may not be revealed.) As will be seen the two first-mentioned curves fall very rapidly from 1939–44. From that year the first curve goes up just as quickly again and the height for 1948 corresponds to that for 1941. The curve for the daily ration together with the amount for canning reaches the same high level in 1945 as for 1940 and 1941, and does not pass that amount. The curves for industry and for the bakeries begin to fall in 1940 and they, too, reach their lowest point in 1944. From that year they are steadily going up. The industry curve in 1948 has exceeded the height of 1940 and before the war. The curve for bakeries has not yet reached more than two-thirds of the pre-war height.

Supposing the rationing of sugar is the main cause, and based on the local factor, we would expect to notice the effect on the teeth from one-half to one year after the change has taken place. This seems to be true during the period of decrease and also for the period of increase in regard to the temporary teeth in the three lowest age-groups. From 1945–46 a distinct increase in caries-affected surfaces is seen (fig. 5). For the age-group 5–6 years the change does not come till 1946 and in children of 6–7 years, not till 1947. The reason for this may be explained simply on the basis of the age of the teeth: the older the teeth the more resistant they are.

This is also evident from Table III which shows that the caries frequency in children of 13-14 years, even in 1948, is still decreasing.

Commenting on the sugar-curves: the daily sugar ration during the whole of the war and up to date has been about 30 grammes per day as an average. Extra amounts for canning and other purposes have varied. The quota for bakeries had diminished in 1944 to one-quarter of that in 1939 and for industry to one-eighth. In 1948 the amount for industry was even higher than before the war. Some of these products, however, are exported. As a consequence of strict rationing, sweet marmalade, pastry, cookies, candy and other sweets were very seldom to be had during the war. Candy and other ordinary sweets were wholly absent from the market the last two years of war. Eating sweets of different kinds, especially between meals, stopped gradually.

Since autumn 1945 there has been no rationing of cookies, pastries, marmalade, canned fruits, berries and juices. A small ration of chocolate and candy has been available for each person every month. In families these rations are usually given to the children. Soon after the war white bread could be bought, but in the spring 1946 the flour extraction was raised to 80% and later to 85%.

Together with these changes in the carbohydrate factor, the consumption of protective food has also been altered. In spite of the fact that the daily consumption of whole milk is greater now than before the war, one cannot be quite sure that the pregnant and nursing mother and the pre-school child take their ration of 0.75 litre just as regularly as they did during the war. Cod-liver oil is not taken to the same extent as before. The consumption of potatoes, carrots and turnips is diminished. The nutritional condition as a whole, however, is much better than during the war.

*It is safe to state that the most pronounced change in food and habit of eating during the war compared with the pre-war period is to be found in the group of refined carbohydrates.* The same is true when we compare the post-war with the war period. The effect of this change on the teeth seems to be a double one, influencing the resistance as well as the factors acting directly.

#### REVIEW OF SIMILAR INVESTIGATIONS

In 1946 the Norwegian Association for Combating Dental Diseases offered a prize for the best essay on the cause of the decrease in caries frequency in Norway during the war. The two prize-winners, Schulerud and Sognnaes, both ascribe the change in dental condition to the reduction of refined carbohydrates—and especially of sugar. The former considers the reduction of sugar wholly as a lowering of the local factor, whereas Sognnaes suggests that the more natural food during the war (as a consequence of the decrease in refined carbohydrates) has given the teeth "something" which has increased their resistance. Alexander, in his analysis of the cause of the caries reduction in Norway during the war, points to the combined effect of better nutrition during the developmental period and the reduced local factor.

In the other Scandinavian countries a reduction in the caries frequency has also been observed.

In Finland an even greater reduction has been found than in Norway. The nutritional condition was poorer than with us, and the ration of sugar and sweets was smaller (Wilksa, Ekman).

In Denmark the caries reduction was not as high as in Norway (Krohn and Pedersen, Pedersen). Here the access to such valuable foodstuffs as milk, cheese, butter, meat and vegetables was much better than in Norway. The ration of sugar and sweets was also higher.

In Sweden only a small reduction in caries frequency was observed (Sandberg, 1946; Maunsbach *et al.*, 1947). Here the nutritional condition was the best among the Northern countries and even better than before the war. The reduction in sugar, cookies and sweets was very small.

A Commission on Caries comprising three members from each of these four countries is studying this very interesting difference in caries reduction in connexion with food and nutritional condition.

Some most interesting material showing the increase in dental health among children during wartime has been collected by May Mellanby and Coumoulos, and Knowles from England. Mellanby and Coumoulos ascribe the reduction in dental caries wholly to the better nutritional condition of the mothers and young children during the war, thus increasing the tooth resistance. Decrease in caries as well as decrease in M-hypoplasia in 5-year-old children was still in progress even in 1947. (The authors do not mention the change in consumption of sugar and sweets.)

Knowles, in her report on the very low caries frequency in children in the Channel Islands at the end of the German occupation, compared with children evacuated to the British Isles, does not draw any conclusion as to the cause. She, too, has found a high increase in caries from 1945 to 1947.

From several other countries, too, directly or indirectly touched by the last war, have come reports of a low caries frequency in children during the war (Schour and Mässler, 1947).

#### ACKNOWLEDGMENT

I wish to extend my sincere thanks to all the school dentists as well as to the staff and the personnel of the Pedodontic Department for valuable help in these investigations. The study has been made possible by grants from the following institutions: Norske Melkeproducenter Landsforbund, A/S Norsk Dental Depot, Ole Smith Houskens Fond, A/S Si-Ko. I am very grateful for these helpful gifts.

#### REFERENCES

- ALEXANDER, E. (1948) *Norske Tandlaegeforen. Tid.*, 58, 357 (English Summary).  
 BENSOW, V. (1919) *Odontol. Tidskr.*, 27, 259.  
 DECHAUME, M. (1946) *Odontologie*, 84, 53.  
 EKMAN, T. (1948) *Tandlaegebladet*, 52, 215.  
 JAY, PH. (1947) *Amer. J. Orthodont.*, 33, 162.  
 KNOWLES, E. M. (1946) *Bull. Min. Hlth.*, August, p. 162.  
 KROHN, C., and PEDERSEN, P. O. (1945) *Acta Odont. scand.*, 6, 129.  
 MAUNSBACH, A., OLINDER, O., and ANDER, P. E. (1947) *Svensk. tands. tidskr.*, 40, 1.  
 MELLANBY, M., and COUMOULOS, H. (1944) *Brit. med. J.* (i), 837.  
 ———, ——— (1946) *Brit. med. J.* (ii), 565.  
 ———, and MELLANBY, H. (1948) *Brit. med. J.* (ii), 409.  
 PEDERSEN, P. O. (1946) *Odontol. Tidskr.*, 54, 379.  
 RAMM, J. (1919) *Norske Tandlaegeforen. Tid.*, 29, 122.  
 SANDBERG, TH. (1946) *Odontol. Tidskr.*, 54, 312.  
 SANNERUD, O. (1945) *Norske Tandlaegeforen. Tidskr.*, 55, 135.  
 SCHOUR, J., and MÄSSLER, N. (1947) *J. Amer. Dent. Ass.*, 35, 1.  
 SCHULERUD, A. (1948) *Munpleien*, No. 1 (English transl. in press, Oslo).  
 SÖGNNÆS, R. F. (1948) *Munpleien*, No. 2.  
 ——— (1948) *J. Nutrit.*, 36, 1.  
 ——— (1948) *Amer. J. Dis. Child.*, 75, 792.  
 WHEATLEY, J. (1920) *Brit. dent. J.*, 41, 753.  
 WIMMENAUER, A. (1933) Quoted according to J. Brun, *Munpleien*, No. 1.  
 WILSKA, A. (1946) *Odontol. Tidskr.*, 54, 296.

## Section of Endocrinology

President—H. GARDINER-HILL, M.B.E., M.D., F.R.C.P.

[November 24, 1948]

**Addison's Disease.**—R. I. S. BAYLISS, M.R.C.P., and RUSSELL FRASER, F.R.C.P.

Housewife, aged 40. July 1948: Admitted to hospital, complaining of lassitude since 1940 and increasing pigmentation since 1944. She had been treated for psycho-neurosis in 1944 and 1948. She had never suffered gastro-intestinal disturbances, there had been no change in menses and no loss of weight. Examination showed generalized pigmentation involving buccal mucosa and nails; axillary hair was scanty. The blood-pressure was 110/70.

*Investigations.*—Kepler's water elimination test, "A" = 100; blood urea 24, chlorides 590, sodium 330, potassium 19, mg.%, glucose tolerance test normal; intravenous insulin tolerance test normal; E.S.R. 4 mm. per hour; E.C.G. low voltage; 17-ketosteroids excretion 1.75 mg. in twenty-four hours; blood-count normal; Cutler-Wilder test: blood-pressure fell from 120/80 to 90/60 after thirty-six hours and patient vomited; blood electrolytes at this time were chlorides 560 mg.%; urea 24 mg.%; sodium 300 mg.%; potassium 23 mg.%. The blood-sugar after eighteen hours' fast was 88 mg.%.

*Adrenotrophic test* (Dr. Prunty, *see* p. 267).—Eosinophils decreased 30% and there was no increase in urinary uric acid/creatinine ratio; i.e. no evidence of adrenal response.

She was given 3 grammes NaCl and 2.5 mg. DOCA daily, which was increased to 6 grammes NaCl and 3.5 mg. DOCA after fifteen days, whereupon the patient's face became œdematous and the blood-pressure rose to 140/84, chlorides to 606 mg., sodium to 321 mg., and the potassium fell to 15 mg.%. Sterile saline was substituted for DOCA and the patient became apathetic and listless again. She was finally treated with testosterone 25 mg. daily with immediate improvement, and has now had 450 mg. testosterone implanted.

The interest in the case lies in the difficulties of confirming the clinical diagnosis and providing substitution therapy, and in the relationship of the psychoneurotic manifestations to chronic adrenal insufficiency. The response to the Cutler-Wilder and adrenotrophic tests and the low excretion of 17-ketosteroids confirm the diagnosis, but some of the functions of the adrenal cortex are not demonstrably abnormal,

e.g. those concerned in the control of electrolyte and carbohydrate metabolism. DOCA was not indicated in the face of normal electrolyte metabolism, and the patient responded well to testosterone.

**Addison's Disease Treated by Adrenal Grafting.**—Shown by A. ELTON, F.R.C.S., for L. R. BROSTER, O.B.E., M.Ch.

W. H., aged 38, male.

2.2.48: Admitted to Charing Cross Hospital under Mr. Broster, to whom he was referred by Dr. N. G. Hulbert from the Metropolitan Hospital, Hackney.

*History.*—Morning vomiting, weakness, dizziness for five years, accompanied by headache and aching in loins. These symptoms became worse from 1943. Has become darker skinned since 1943, also had lost weight until he came under treatment. Appetite poor. Some increased frequency of micturition; M.N. 2-3. Cramp in limbs and abdominal muscles.

*Personal history.*—Tonsillitis, influenza, exanthemata. No past history of tuberculosis.

*Family history.*—No history of tuberculosis or Addison's disease.

*On examination.*—Lightly built, looks fit. Skin of whole body is pigmented a deep brown colour. Intelligent, alert and lively—no evidence of loss of weight. Buccal cavity: Palate pigmented. No oral sepsis. Teeth good. Thyroid normal. Chest, C.V.S.: N.A.D. Blood-pressure 115/70. Abdomen: N.A.D. Limbs: Muscular power good.

This was the clinical picture at this time, the treatment at the Metropolitan Hospital having been:

(1) Daily DOCA injections at first, then decreased to an injection every three days.

(2) Implant of  $3 \times 50$  mg. DOCA tablets on 12.7.47 and of  $4 \times 100$  mg. DOCA tablets on 3.9.47.

(3) 16 grammes salt per day until November 1947 when it was reduced to 4 grammes per day.

Blood group A. Rh-negative.

2.2.48: Further investigations on admission to Charing Cross Hospital: X-ray chest and abdomen, N.A.D.

18.3.48: Admitted to Woburn Clinic for operation, where a suitable "donor" of Group II virilism was available.

29.3.48: Pre-operative treatment of patient W. H.:

(1) Intravenous transfusion of glucose saline, 4-3% glucose and 18% salt.

(2) Eucortone 10 c.c. intravenously.

(3) DOCA 1 c.c. (5 mg.) intramuscularly.

*Operations by Mr. L. R. Broster.*—A general anaesthetic was given by Dr. R. J. Clausen, and an operation for left adrenalectomy was performed on the "donor". The adrenal vein was found with some difficulty and was removed with the gland. The adrenal itself was triangular in shape and about twice the normal size. It was placed in a bowl of warm normal saline after being flooded with heparin solution.

*Operation on W. H. under local anaesthesia.*—The left rectus sheath was exposed by a diagonal skin incision in its lower third. It was opened and the rectus muscle

retracted medially, exposing the deep epigastric vessels. These were divided and the distal end ligatured. The spurting proximal end was flooded with heparin. The deep epigastric artery was small and had two venae comites which could not be dissected free. A length of 6/0 catgut, threaded on two long straight needles, was passed through the vessels.

The adrenal graft was once more flooded with heparin through the stump of the adrenal vein. The needles were passed up the vein and through the substance of the gland, drawing the bleeding stump of the deep epigastric vessels well inside, and the suture tied on the convex surface of the gland.

The graft was tucked medially under the rectus which was allowed to fall into its normal position. The wound was closed in layers by interrupted catgut sutures.

*Post-operative care (see Discussion (para 3)).*—The blood-pressure during operation and immediately afterwards was maintained at 140/80 mm.Hg.

2.4.48: Readmitted to Charing Cross Hospital.

He was allowed up on the seventh day. The skin sutures were removed on the eighth day. His blood-pressure was recorded as follows (*see Table I*).

TABLE I.—BLOOD-PRESSURE READINGS

| Date    | Blood-pressure reading | Comment                                                                                                                    |
|---------|------------------------|----------------------------------------------------------------------------------------------------------------------------|
| 3.5.47  | 110/80                 | Reading when case first seen at Metropolitan Hospital.                                                                     |
| 2.2.48  | 115/85                 | Admission to Charing Cross Hospital. No treatment since DOCA implant five months ago.                                      |
| 23.2.48 | 110/65                 | Beginning to fall; implant running out.                                                                                    |
| 4.3.48  | 95/70                  | Further fall.                                                                                                              |
| 6.3.48  | 140/80                 | DOCA 2 c.c. daily commenced four days previously, now taking effect.                                                       |
| 14.3.48 | 140/80                 | Level maintained on DOCA 1 c.c. daily.                                                                                     |
| 29.3.48 | 140/80                 | Day of operation.                                                                                                          |
| 31.3.48 | 110/90                 | Rapid fall forty-eight hours post-operatively despite eucortone 10 c.c. four-hourly.                                       |
| 1.4.48  | 140/80                 | Rise after an extra 20 c.c. eucortone.                                                                                     |
| 2.4.48  | 118/76                 | Readmission to Charing Cross Hospital. DOCA 2 c.c. daily re-commenced.                                                     |
| 5.4.48  | 160/110                | DOCA dosage excessive now that graft is taking over. DOCA now stopped.                                                     |
| 15.4.48 | 115/70                 | Steady level now maintained without DOCA, eucortone or salt.                                                               |
| 18.4.48 | 94/70                  | Fall coinciding with deterioration in condition over past few days. DOCA 2 c.c. every three days and salt 4 grammes daily. |
| 9.5.48  | 115/80                 | Blood-pressure steady on DOCA 2 c.c. weekly. Salt intake 4 grammes daily. Discharged and DOCA finally stopped.             |

Condition satisfactory. Blood-pressure 170/98. Abdomen: Adrenal gland palpable under operation scar. No tenderness. Patient apyrexial. DOCA continued 2 c.c. daily.

Serum values were as follows:

|                                      | Chlorides mg. % | Sodium mg. % | Potassium mg. % | Date    |
|--------------------------------------|-----------------|--------------|-----------------|---------|
| <i>Before any treatment</i> .. ..    | 335             | 275          | 25              |         |
| <i>After implant and during DOCA</i> |                 | 315          | 15.6            | 26.2.48 |
| <i>and salt administration</i> ..    |                 | 319          | 17.9            | 3.3.48  |
|                                      |                 | 321          | 16.7            | 9.3.48  |
| <i>After operation</i> 20.3.48 .. .. | 579             | 335          | 16.2            | 9.4.48  |
|                                      | 576             | 318          | 15.7            | 5.5.48  |

Thus the serum values have remained at a normal level after operation on a minimal dose of DOCA which was later stopped altogether.



*Postscript.*—Patient is now doing heavy work as a Head Porter. Serum values on 2.2.49 were: sodium 329, potassium 19.5 and chlorides 610 mg.%. These values are normal for this patient, who has had no DOCA for nine months and no salt for seven months. His blood-pressure is normal.

### DISCUSSION

A case of Addison's disease treated by adrenal grafting. The treatment of this case was largely empirical and experimental. Nevertheless the following conclusions can be drawn from this and other similar cases:

(1) *Before operation* the patient must be balanced on eucortone, DOCA, salt and glucose, as shown by normal blood sugar, serum values and blood-pressure readings. He should be feeling fit; especial attention is drawn to the importance of maintaining a normal blood-sugar curve: these patients tend to die in hypoglycæmia.

An intravenous glucose-saline drip is put up before operation. Premedication: nembutal 3 grains, atropine 1 100 grain, one hour pre-operatively, no morphine.

(2) *The operation* itself has been fully described. The use of heparin is important as it prevents thrombosis. A syringe filled with 20 c.c. eucortone should be kept ready during operation, should the patient go into crisis.

(3) *Post-operatively*, we have prevented an Addison's crisis occurring (and these patients very easily go into crisis) by the following measures:

*First forty-eight hours after operation.*—(a) 20 c.c. eucortone intravenously immediately after operation and 10 c.c. given intravenously six-hourly for forty-eight hours.

(b) 2 c.c. DOCA intramuscularly six-hourly for forty-eight hours.

(c) 4 grammes salt by mouth—as salt drinks or effervescent tablets, daily.

(d) Glucose drinks *ad lib*.

(e) Keep patient on intake and output chart. Keep chart balanced. Keep urinary output at least at 1,500 c.c. per twenty-four hours.

(f) Keep four-hourly blood-pressure chart and half-hourly pulse chart. Give 20 c.c. eucortone if blood-pressure falls markedly.

*After forty-eight hours.*—10 c.c. eucortone intravenously, 2 c.c. DOCA intramuscularly twice daily, for three days. Stop drip. Continue salt and glucose as before.

*After this three-day period.*—Stop eucortone. Give DOCA 2 c.c. daily intramuscularly, gradually diminishing the dose to 2 c.c. three times weekly and then 1 to 2 c.c. weekly, and stopping it after one to two months. Continue salt for at least two to three months—4 grammes daily.

**Simmonds' Disease following Hæmatemesis. Gastric Ulcer.**—Q. HOBSON, B.M., M.R.C.P., and RUSSELL FRASER, F.R.C.P.

Housewife, aged 50. 1931: She had hæmatemeses, following which she complained of amenorrhœa and progressive thinning of body hair. She did not regain her previous weight, and continued to suffer recurrent bouts of dyspepsia.

On examination in May 1947, she was a thin woman, with dry skin, and scanty axillary and pubic hair, small breasts, with hypoplastic uterus and genitalia. The blood-pressure was 106/60.

While in hospital she had several attacks of faintness, and during one attack the blood sugar was found to be 57 mg.%. }

*Investigations.*—Barium meal: Small gastric ulcer on the lesser curve. B.M.R. — 23%; — 13%. Insulin tolerance test showed a rapid fall and abnormally slow rise; 17-ketosteroids excretion 2.0 mg. and 1.2 mg. in twenty-four hours.

Since May 1947 the patient has been greatly improved by treatment with thyroid and stilbæstrol and latterly by implantation of testosterone and DOCA.

*Comment.*—When the patient was admitted to hospital in 1931, it is recorded that she had severe and recurrent hæmatemeses. From this time the symptoms and signs of Simmonds' disease developed. She did not seek medical advice for these complaints until fourteen years later, when symptoms of anxiety and depression coupled with attacks of hypoglycæmia caused her admission to a hospital for psychiatric investigation.

This patient was not pregnant at the time of onset of her illness, nor was there evidence of any local pituitary, or general disease. The hæmatemeses appear to be the only precipitating factor causing the subsequent development of Simmonds' disease. We have found no previous record of Simmonds' disease following hæmatemeses in the literature.

#### Post-traumatic Pan-hypopituitarism.—A. STUART MASON, M.B., M.R.C.P.

Male, aged 23.

*History.*—Always fit and well with normal development in puberty until four and a half years ago. At that time sustained a fracture of the base of the skull in a lorry accident. Was fourteen weeks in hospital. Found that he had no energy, was slowing up both mentally and physically. These symptoms have continued. Persistent lassitude and weakness. Complete loss of libido. Has gained 2 st. in weight, and has noticed that his face has become very pale and puffy. Used to shave daily, since the accident this has dropped to once in three weeks.

March 1948: He developed a dental abscess, and although the infection was not severe he lapsed into a drowsy comatose state, with much vomiting. Blood-pressure 95/60 at this time.

July 1948: Investigated in hospital.

*On examination.*—Pale lethargic young man. Fine soft skin, but puffy face and hands. Scalp hair normal. Eyebrows thin at outer third. Face and body hair very scanty. B.P. ranged from 95/60 to 120/90. 17-ketosteroids—1 mg./twenty-four hours. B.M.R. — 28%. Radio-iodine excretion showed evidence of thyroid hypofunction. Fasting blood sugar—72 mg. per 100 c.c. Insulin sensitivity test—increased sensitivity. X-ray of skull—small bony thickening in floor of sella turcica. 600 mg. of testosterone implanted. Marked improvement followed on this.

#### Thyrotoxicosis, Exophthalmic Ophthalmoplegia, Myasthenia Gravis and Vitiligo.—RAYMOND GREENE, D.M.

Woman aged 27 with one child.

*History.*—She was perfectly normal until December 1946 when she began to complain of fatigue and breathlessness on exertion. In February 1947 she first noticed occasional diplopia, which got worse as the day wore on and which steadily increased. In April 1947 exophthalmos began in the right eye and she first noticed a patchy brown pigmentation of the skin. The complete classical syndrome of thyrotoxicosis rapidly developed and treatment with thiouracil began in May 1947. In June 1947 ptosis of the left eye was first observed. In July weakness began in the right arm and in August this was followed by weakness of the left arm and both legs.

Between the onset of the disease in December 1946 and May 1947 she lost 2 st. in weight, regaining most of this while under treatment with thiouracil. All symptoms were greatly improved during this treatment.

When first seen by me in October 1947 she showed a bilateral exophthalmos, more severe on the right side, with ptosis of the left upper lid. There was extreme weakness of the muscles of the arms and legs, especially of the extensors, but no muscle wasting. There was a typical myasthenic smile. There was a patchy brown pigmentation of the skin of both legs and arms and to a lesser degree of the abdomen. The pulse-rate was 80 and the B.P. 125/85. The hands were warm but dry and there was a slight tremor. There was a diffuse soft enlargement of the whole thyroid, especially of the right lobe. X-ray of the chest was normal. Eye movements at this time are shown in the following table:

*Eye Movements when First Shown to Section, on 22.10.47 (fig. 1)*

|        |    |    | Without prostigmin |        | With prostigmin |        |
|--------|----|----|--------------------|--------|-----------------|--------|
|        |    |    | R.                 | L.     | R.              | L.     |
| Up     | .. | .. | Weak               | Absent | Normal          | Normal |
| Down   | .. | .. | Absent             | Absent | Normal          | Normal |
| In     | .. | .. | Weak               | Weak   | Normal          | Normal |
| Out    | .. | .. | Absent             | Absent | Absent          | Absent |
| Ptosis | .. | .. | Absent             | Severe | Absent          | Absent |
|        |    |    | (lid retraction)   |        |                 |        |

*Eye Movements after Thyroidectomy (figs. 2 to 5)*

|        |    |    | Without prostigmin  |        | With prostigmin |        |
|--------|----|----|---------------------|--------|-----------------|--------|
|        |    |    | R.                  | L.     | R.              | L.     |
| Up     | .. | .. | Weak                | Absent | Normal          | Normal |
| Down   | .. | .. | Absent              | Absent | Normal          | Normal |
| In     | .. | .. | Weak                | Weak   | Normal          | Normal |
| Out    | .. | .. | Weak                | Weak   | Weak            | Weak   |
| Ptosis | .. | .. | Slight              | Severe | Absent          | Absent |
|        |    |    | (no lid retraction) |        |                 |        |

(Unchanged except that outward movements were now present though weak and the disappearance of R. lid retraction has unmasked a latent R. ptosis.) Note pigmentation (fig. 6).

An injection of 2.5 mg. of prostigmin produced complete disappearance of the ptosis and of the weakness of the limbs and facial muscles. Movement of the right eye became normal except for outward movements. Movement of the left eye also became normal except for outward movements. In short, myasthenic symptoms were entirely relieved except for those due to weakness of the external recti. The hypothesis was advanced that the patient showed a combination of myasthenia gravis with thyrotoxicosis, all muscular weakness except that of the external recti being due to the former and that of the external recti to the latter.

On October 24, 1947, after preparation with Lugol's solution, a subtotal thyroidectomy was performed by Mr. J. E. Piercy. Both lobes were found to be enlarged, vascular and friable. The inferior thyroid arteries, which were large, were ligated. After operation the signs of thyrotoxicosis were absent. The prostigmin requirements of the patient rose from 1 tablet three times a day to 2 tablets three-hourly. This dose, as before, controlled the majority of the signs of myasthenia and movement was for the first time observed in the outward direction in both eyes. The improvement in the action of the external recti continued though it did not become perfect. It was unaffected by prostigmin.

On November 19, 1947, thymectomy was performed by Mr. Piercy. The thymus was found to be fleshy and enlarged, the weight being 18.5 grammes. Within one

FIGS. 2-6.—After thyroidectomy.



FIG. 1.—Before treatment, looking straight forward. Slight exophthalmos  $R > L$ . R. upper lid retraction. L. ptosis.



FIG. 2.—Looking down. No downward movement R. or L. Disappearance of R. upper lid retraction, and appearance of slight ptosis. Exophthalmos unaffected. L. ptosis unaffected.

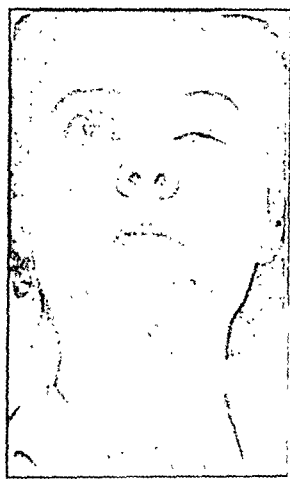


FIG. 3.—Looking up. Right eye weak. Left eye immobile.



FIG. 4.—Looking left. Weak inward movement of right eye. Left eye shows very slight outward movement.



FIG. 5.—Looking right. Weak inward movement of left eye. Right eye shows very slight outward movement.

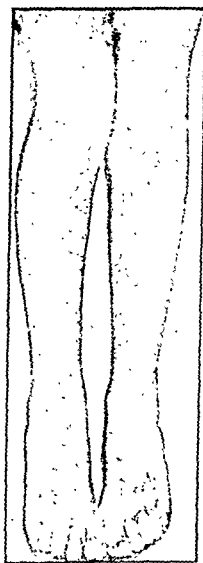


FIG. 6.—Note pigmentation.

FIGS. 7-12.—One year after thymectomy.



FIG. 7.—Looking left.  
Slight residual weakness  
of left external rectus.



FIG. 8.—Looking right.  
Very slight residual weak-  
ness of right external rectus.



FIG. 9.—Looking forward.  
No ptosis or lid retraction.  
The slight right internal  
strabismus shown in the  
photograph has not been seen  
on other occasions.



FIG. 10.—Looking up.  
Normal movement.



FIG. 11.—Looking down.  
Normal movement.

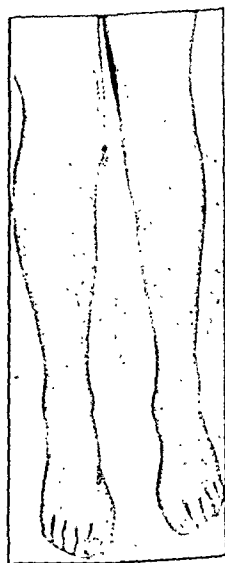


FIG. 12.—Condition one  
year after operation. Pig-  
mentation reduced.

*Eye [Movements after Thymectomy, Assisted by a Smaller Dose of Prostigmin*

All movements normal except for weakness of both external recti and occasional L. ptosis of a slight degree. No change in degree of exophthalmos. Weakness of skeletal and facial muscles eliminated. (figs. 7 to 11). Slight improvement in pigmentation (fig. 12).

week it was possible to reduce the dose of prostigmin, from 2 tablets three-hourly immediately after operation, to 1 tablet three-hourly. A steady improvement in all myasthenic symptoms occurred and by December 4 an examination conducted four hours after the last dose of prostigmin, showed all movements to be normal except for slight persisting weakness of the external recti.

The patient was discharged on December 5, 1947, taking by this time  $\frac{1}{2}$  tablet of prostigmin every two hours. On January 20, 1948, a further improvement had occurred and four hours after prostigmin all eye movements were normal except for outward movement of the left eye, which was still weak. Two patches of alopecia areata had occurred on the scalp. She complained of occasional diplopia when looking to the left.

When seen in March 1948 she was no longer having diplopia or any other symptoms. All eye movements were normal except for outward deviation, especially of the left eye. Both eyes could, however, be moved almost normally when she made a really concentrated effort. 1½ tablets were prescribed. The alopecia areata had gone and the pigmentation had disappeared. In August 1948 she was taking 4 tablets of prostigmin a day, which kept her completely symptom-free. No signs of myasthenia gravis were present on examination of the tongue and no signs of thyrotoxicosis, except the slight persistent weakness of the external recti. There was no ptosis.

It is difficult exactly to evaluate the part played by thymectomy in her improvement. Before the operation the optimal dose of prostigmin was 6 tablets a day and it has been reduced only to 4 tablets a day. On the other hand the patient is convinced that this slight alteration in prostigmin requirements does not give the true picture of the improvement which she has experienced. Continued observation has supported the original hypothesis that myasthenia gravis is responsible for the weakness of all muscles other than that of the external recti. The weakness of other muscles could be abolished by prostigmin. Both before and after the two operations, weakness of the external recti was unaffected by prostigmin.

*Pathological reports.*—The *thyroid*, which weighed 58.5 grammes, showed a moderate, diffuse epithelial hyperplasia with decrease in colloid and occasional areas of lymphadenoid infiltration. The *thymus*, which weighed 18.5 grammes, was characteristic of myasthenia gravis and showed hemorrhage into cavernous angiomatous spaces, which were probably lymphatic spaces.

#### DISCUSSION

Two points in this case are worthy of special note. In the first place the "see-saw" relationship between thyrotoxicosis and myasthenia gravis so commonly described is absent. No significant increase of the myasthenia occurred after thyroidectomy, though there was a slight temporary increase in prostigmin requirements. In the second place, external rectus palsy, which was unaffected by prostigmin and was therefore assumed to be due to exophthalmic ophthalmoplegia, improved steadily after thyroidectomy and did not, as might be expected, become worse.

**The Use of Adrenocorticotrophin in Testing for Adrenal Insufficiency.**—F. T. G. PRUNTY, M.A., M.D., M.R.C.P.

The experiments on which this report is based were conducted with Professor G. W. Thorn and Dr. P. H. Forsham at Harvard. It is well known that adrenocorticotrophin is capable of stimulating the adrenal cortex, one result of which is a lysis of lymphoid tissue and a reduction of circulating lymphocytes (Dougherty and White, 1947). It is also known that compound A of Kendall (11-dehydrocorticosterone) will produce an increase of uric acid excretion (Forsham *et al.*, 1946).

Experiments in the normal human indicated that within a few hours of a single injection of adrenocorticotrophin (25 mg.) the following effects could be elicited: (1) A marked fall in circulating lymphocytes. (2) An increase in uric acid excretion. These effects are elicited by the secretion of the adrenal cortex in response to stimulation by the trophic hormone. Therefore adrenocorticotrophin should not produce such a response in Addison's disease, and was found not to do so (fig. 1). Injection of 17 mg. of the cortical hormone, compound "F" (17-hydroxycorticosterone), however, produced a response in Addison's disease (fig. 1) which is comparable with the response obtained in the normal individual by the injection of pituitary adrenocorticotrophin. This effect could not be produced with desoxycorticosterone or testosterone (Forsham *et al.*, 1948).

During the counting of the differential films for lymphocyte estimations it was observed that the eosinophils disappeared completely. The direct counting of eosinophils in a chamber being much easier than differential counts, this effect was followed up and curves produced such as that in fig. 1. Patients with Addison's disease show a very marked fall of eosinophils with compound "F" and not with adrenocorticotrophin. By contrast the pituitary hormone produces this response also in the normal individual.

Study of the time factors involved showed that the maximum response in the eosinophil count occurred four hours after the intramuscular injection of adrenocorticotrophin and that the maximum rate of uric acid excretion occurred during the last three of the four hours after the injection. Both short and long term experiments with adrenocorticotrophin have shown that there is no effect on the quantity of creatinine excreted. These results are also shown with the experiments employing compound "F" (fig. 1). Accordingly the concentration of creatinine

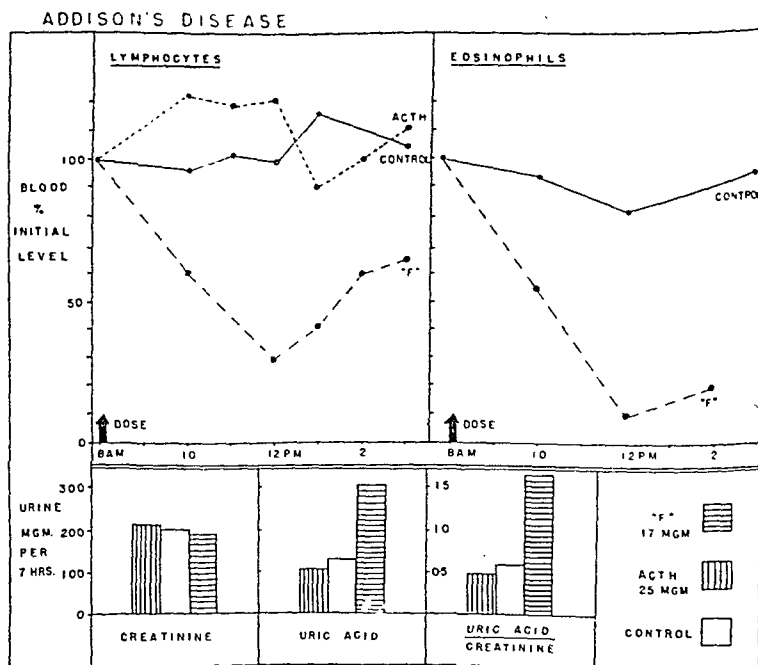


FIG. 1.—The response of a male patient with Addison's disease to 25 mg. ACTH, I.M. or 17 mg. compound "F" (17-hydroxycorticosterone). 25 mg. of ACTH given to a normal individual produces responses comparable with those given by compound "F" in this patient. "Control" refers to a control experiment.

in urine specimens can be used as a reference point, the amount of uric acid excreted being calculated relative to this. Thus may be avoided the necessity for accurate collections of urine and the careful measurement of volumes which is an important source of error during a short collection. Accordingly a test was standardized on these data as follows:

(1) Two-hour collections of urine after an overnight fast. Uric acid and creatinine concentrations are measured and expressed as a ratio  $\frac{\text{Uric acid}}{\text{creatinine}}$

(2) A blood specimen is taken into a tube containing Wintrobe's anticoagulant. An eosinophil count is done and the uric acid concentration in the plasma measured.

(3) At this time 25 mg. adrenocorticotrophin is injected intramuscularly.

(4) Urine is voided one hour after injection, and again four hours after injection. The uric acid/creatinine ratio is measured in the specimen passed between the first and fourth hours.

(5) Four hours after injection another blood sample is taken and the above observations made.

The increase in the uric acid/creatinine ratio after the adrenocorticotrophin is customarily expressed as a percentage of the initial ratio. This increase in uric acid excretion naturally depends upon adequate renal function and knowledge of the Van Slyke urea clearance may be helpful in assessing the response. In conditions where the adrenal cortex is in a supernormally active state the "fasting" uric acid/creatinine ratio may be abnormally high and there may also be difficulty on the part of the kidney to increase the clearance of uric acid. For this reason an adequate urine flow is maintained during the test and observation of the plasma uric acid level is helpful in assessing the response. With adequate clearance of uric acid it is

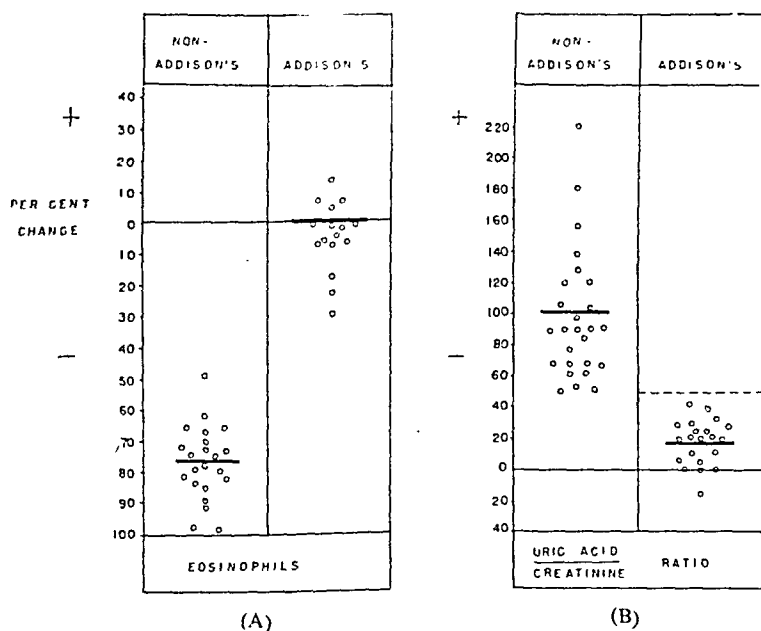


FIG. 2.—The response in (A) blood eosinophil count and (B) urinary uric acid/creatinine to 25 mg. ACTH (for details see text). The diagram shows the results with 26 hospital patients without and 21 patients with Addison's disease in (B), and 22 without and 16 with Addison's disease in (A).



usual for a small fall to occur in this figure after four hours whereas if uric acid excretion is impaired a definite rise will be observed.

The response by the eosinophils is expressed as the percentage fall from the resting level. Values obtained with this test are summarized in fig. 2.

(It should be noted that severe cases of hypopituitarism may also fail to respond to a single dose of adrenocorticotrophin.)

The observations referred to above concerning the type of cortical hormones producing a response in Addison's disease would, together with other evidence, indicate that this test is most closely correlated with an "11-oxysteroid" effect and differs in this respect from other diagnostic tests used in Addison's disease which are primarily connected with desoxycorticosterone-like activity. It has the further advantage that the eosinophil response is independent of renal function.

This test was carried out on the patient of Drs. Fraser and Bayliss (*see* p. 259). The "fasting" uric acid/creatinine ratio was observed to be 0.39 compared with an average normal of 0.49. There was no increase in the ratio after adrenocorticotrophin, the figure being still 0.39. The plasma uric acid was 2.9 and 2.7 mg. respectively at the beginning and end of the test. The fasting eosinophil count was 91/c.mm. and fell to 64/c.mm. after adrenocorticotrophin, giving a decrease of only 30%. This test was therefore positive, and in accord with the clinical findings. This experience affords a further instance of a positive result with adrenocorticotrophin in the presence of a negative Kepler test.

#### REFERENCES

- DOUGHERTY, T. F., and WHITE, A. (1947) *J. lab. Clin. Med.*, **32**, 584.  
FORSHAM, P. H., THORN, G. W., BERGNER, G. E., and EMERSON, K. (1946) *Amer. J. Med.*, **1**, 105.  
—, —, PRUNTY, F. T. G., and HILLS, A. G. (1948) *J. clin. Endocrinol.*, **8**, 15.

## Section of Orthopædics

President—H. J. SEDDON, M.A., D.M., F.R.C.S.

[November 2, 1948]

Engelmann's Disease.—L. S. MICHAELIS, M.D.

[The first adult case of this rare condition and the first to be published from this country.]

Miss B. M., aged 24.

*History.*—Normal birth. Breast-fed. First teeth late. Standing and walking at age of 2. Ache in legs when 3 years old. At school exempt from games because of weakness, lordosis and knock-knees. No serious diseases but always delicate. Slight accidents but no fractures. Parents healthy. Brother, 32, under treatment at Children's Hospital between ages of 2 and 7—no records obtainable, no X-rays taken—walks with a limp, but served in the war. Declines to attend for examination.

*Symptoms.*—No pain, occasional ache in hip region. Unable to stand, walk, run or kneel for long, but has kept domestic post for seven years.

*Signs.*—Under middle height, thin, pale, with blue hands and feet. Moustache on high upper lip. Small hands and feet, long thighs. The main bulk of arms and legs made up by *thickened bones*, covered by *weakly developed muscles*. Slight lumbar lordosis with hair over lower lumbar spine, *knock-knees* and valgus ankles. Muscular power weak. No neurological signs. Liver, spleen not enlarged. All joint movements free. *Gait* resembles the uncertain gait of patients with muscular dystrophy rather than actual waddling. Periods normal. Above average intelligence; precise; said to have told purposeless lies during last year or two.

*X-rays.*—Symmetrical sclerosis of anterior parts of inner table of skull and the base of middle and anterior fossa. Symmetrical hyperostosis and sclerosis, elongation and slight bending of diaphyses of long bones (figs. 1 to 5).

*Blood examination.*—Slight anæmia, no lymphocytosis. Monocytes 7%.

*Calcium balance.*—Low normal level.

*Serum calcium, plasma phosphorus, serum phosphatase (alk.).*—Normal.

This patient shows X-ray changes identical with those first described by Engelmann (1929) in a boy of 8. He called the condition "Osteopathia hyperostotica (sclerotisans) multiplex infantilis. ? Hæmatogenes." That it might be due to a blood disease and represent its healing stage, was, admittedly, a guess based on his findings of a possibly enlarged spleen, a lymphocytosis of 40.5%, an increase in monocytes—as in our case—and of eosinophils.

Sear (1948) was the first to direct attention to Engelmann's paper. His patient, a boy of 10, showed no X-ray changes in the skull, but, instead, involvement of the first cervical vertebra, of the clavicles, scapulæ and pelvis apart from the long bones.

Riley and Shwachman (1943) and Neuhauser, Shwachman, Wittenborg and Cohen (1948) describe one boy and one girl of 4 in the first paper, follow them up in their second paper and add two more cases of girls, one 4 years of age and one followed from her 6th to her 18th year. Two of their patients show involvement of clavicles and the long bones, the two others of the base of the skull and the long bones. While Sear was unable to find specific histological changes, the American authors describe and depict absence of normal bone-structure in cortical areas which indicates high osteoblastic and osteoclastic activity. They call the condition "Progressive diaphyseal dysplasia" and, in a postscript, refer to the papers of Engelmann and Sear.

usual for a small fall to occur in this figure after four hours whereas if uric acid excretion is impaired a definite rise will be observed.

The response by the eosinophils is expressed as the percentage fall from the resting level. Values obtained with this test are summarized in fig. 2.

(It should be noted that severe cases of hypopituitarism may also fail to respond to a single dose of adrenocorticotrophin.)

The observations referred to above concerning the type of cortical hormones producing a response in Addison's disease would, together with other evidence, indicate that this test is most closely correlated with an "11-oxysteroid" effect and differs in this respect from other diagnostic tests used in Addison's disease which are primarily connected with desoxycorticosterone-like activity. It has the further advantage that the eosinophil response is independent of renal function.

This test was carried out on the patient of Drs. Fraser and Bayliss (*see* p. 259). The "fasting" uric acid/creatinine ratio was observed to be 0.39 compared with an average normal of 0.49. There was no increase in the ratio after adrenocorticotrophin, the figure being still 0.39. The plasma uric acid was 2.9 and 2.7 mg. respectively at the beginning and end of the test. The fasting eosinophil count was 91/c.mm. and fell to 64/c.mm. after adrenocorticotrophin, giving a decrease of only 30%. This test was therefore positive, and in accord with the clinical findings. This experience affords a further instance of a positive result with adrenocorticotrophin in the presence of a negative Kepler test.

#### REFERENCES

- DOUGHERTY, T. F., and WHITE, A. (1947) *J. lab. Clin. Med.*, **32**, 584.  
FORSHAM, P. H., THORN, G. W., BERGNER, G. E., and EMERSON, K. (1946) *Amer. J. Med.*, **1**, 105.  
—, —, PRUNTY, F. T. G., and HILLS, A. G. (1948) *J. clin. Endocrinol.*, **8**, 15.

It is likely that further cases have been described or observed under different names, e.g. Hirsch (1929), in a paper on osteodystrophia fibrosa, shows X-rays of a child aged 1 year which appear to belong to this group.

The cause of these changes is unknown but a congenital rather than an acquired origin is likely. Syphilis has been excluded in all instances, so has heredity, but the fact that the brother of our patient—unfortunately not accessible—has a disturbance of gait and a history of prolonged illness in early childhood leaves the possibility of occasional familial tendency open.

The lack of decisive changes in the blood chemistry is remarkable when the extent of the visible bone changes is taken into account. Radiologically significant is the symmetry, the exclusive involvement of the diaphyses of the long bones, while metaphyses and epiphyses are not involved and rather show hypostosis, and the "alternative" combinations with changes either in the skull or in the clavicles.

In the absence of reliable data for its cause the condition might best be called "Engelmann's disease" rather than long descriptive names.

#### ACKNOWLEDGMENTS

I am very grateful to Dr. E. B. Hawes who sent this patient to see me, to Sir Thomas Fairbank who generously helped at every stage of the investigation, to Mr. St. J. D. Buxton and Dr. J. D. Gray for granting the facilities of King's College Hospital and carrying out various examinations, and to Drs. D. A. Imrie and F. C. Golding who first directed attention to Sear's paper and provided the films.

#### REFERENCES

- ENGELMANN, G. (1929) *Fortschr. Röntgenstr.*, 39, 1101.  
 HIRSCH, T. S. (1929) *Radiology*, 13, 44 (figs. 51-55, pp. 63-65).  
 NEUHAUSER, SHWACHMAN, H., WITTENBERG and COHEN (1948) *Radiology*, 51, 11.  
 RILEY, C. M. S., and SHWACHMAN, H. (1943) *Amer. J. Dis. Child.*, 66, 150.  
 SEAR, H. R. (1948) *Brit. J. Radiol.*, 21, 236.

Pathological Fracture Through a Cyst of Scapula.—J. F. PAXTON, F.R.C.S.Ed. (for St. J. D. BUXTON, F.R.C.S.).

A. S., aged 35.

*History*.—First seen on April 28, 1948, when she complained that she had strained her right arm ten months previously, while pulling a pram up some steps, and after-

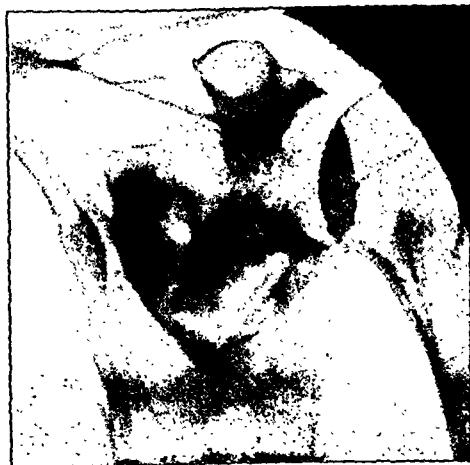


FIG. 1.—X-ray shows fracture into a cyst of the body of the scapula.



FIG. 1.

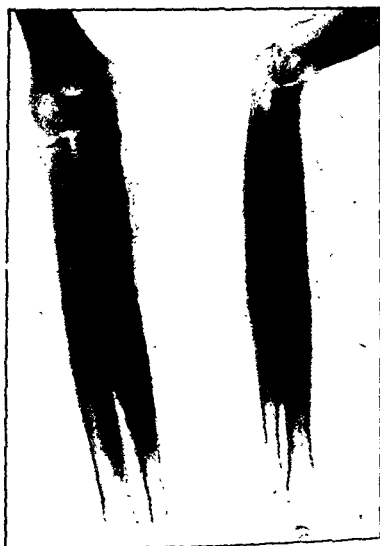


FIG. 2.

FIG. 1.—Note density of frontal inner table and base.

FIG. 2.—Right elbow and forearm (A.P. and lateral views). Note involvement of proximal two-thirds of radius and ulna; distal one-third and wrist free. The left forearm shows identical changes. Both humeri are involved, small bones of hands and feet are free. There are no changes in the spine, clavicles, scapula or pelvis.



FIG. 3A.



FIG. 3B.

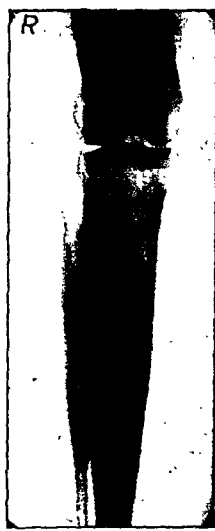


FIG. 4.



FIG. 5.

FIGS. 3A and 3B.—Right and left femur. Note symmetry, dense hyperostosis of diaphysis; head, neck and trochanter free.

FIG. 4.—Right knee and leg, A.P. Note involvement of diaphysis of tibia and fibula. The left side shows identical changes.

FIG. 5.—Left leg and ankle (lateral). Note involvement of proximal two-thirds of tibia; distal one-third and ankle-joint free.

25.6.48: Plastic cast inserted into proximal row of carpus. Wrist immobilized in plaster for two weeks and commenced active wrist movements.

6.10.48: Figs. 3 and 4 show condition on this date.



FIG. 3.

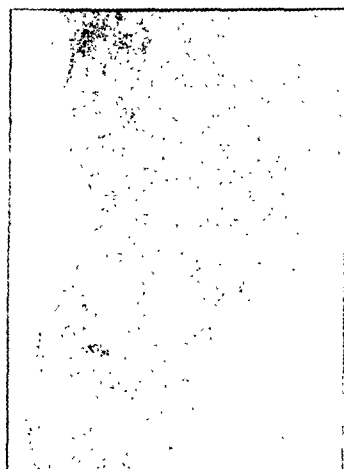


FIG. 4.

FIGS. 3 and 4.—After insertion of plastic case, radiographs taken on 6.10.48.

#### Rupture of Tuberculous Paravertebral Abscess into Pleural Cavity.—M. ALBERT, F.R.C.S.

Female, aged 27.

*History.*—June 1947: She first noticed pain and stiffness in the middle of the back. February 1948: Her spine was manipulated at another hospital, and two months later, when she was seen in the Middlesex Hospital, a radiograph showed tuberculosis of the eighth and ninth thoracic vertebræ with long paravertebral abscess shadows extending from T.4 to L.1 (fig. 1). The lung fields were clear (fig. 2).

10.5.48: Open-air treatment was instituted and she was placed in a plaster bed. The E.S.R. (Wintrobe) was 46 mm. in the first hour, and her temperature fluctuated from normal to 99° F.

21.6.48: She complained of a dry cough and a sharp pain in the right costal margin, made worse on breathing. Temperature 102°+ and signs of a right pleural effusion confirmed by X-ray which also showed some collapse of the right lower lobe (fig. 4). The right paravertebral abscess shadow had disappeared (fig. 3).

1.7.48: Aspiration of the right chest posteriorly yielded turbid yellow fluid containing numerous lymphocytes, and tubercle bacilli were found on culture.

The temperature settled in about three weeks (fig. 5) and her general and local condition have since improved. In December 1948 she was afebrile, the E.S.R. was 15 mm. in the first hour, and the affected vertebræ were recalcifying. The residual fluid in the right pleural cavity was loculated posteriorly and much decreased in amount following repeated aspiration of thick fluid with shreds of lymph coagulum containing numerous necrotic lymphocytes; and the lower edge of the right paravertebral abscess became visible again as the wall thickened.

The recent literature contains several references to the rupture of paravertebral abscesses into (a) The pleura: Seddon, 1936; Starkie, 1938; Enrolaev, 1939; Brooks, 1942. (b) The bronchi: Imbuchi, 1937; De Lucchi, 1940. (c) Oesophagus: Seddon, 1936. (d) Oesophageal diverticulum: Brand, 1939. (e) The aorta: Somerville and

wards had considerable bruising in her right shoulder region. She complained that she could not get her hand right above her head.

She had had a neuritis of right ulnar distribution, which was treated in St. Thomas's Hospital in 1937, by transposition of her ulnar nerve, but this gave no improvement.

*Examination* showed that movements of the shoulder-joint were full, but her right scapula was very prominent, especially along the vertebral border, and rotation of the scapula was limited by about ten degrees on full abduction of the arm. X-ray taken on 28.4.48 showed a comminuted fracture through a cyst of her right scapula. She was seen again on October 7, when she had some pain behind her shoulder, but full movement. X-ray showed very little change in the cyst of her scapula, and no evidence of cervical rib or of any bony injury to the right elbow-joint, which might account for the neuritis involving her right hand.

**Dr. I. H. Milner:** When I examined this patient I found evidence of a right Horner's syndrome, some hypalgesia in the neck and more atrophy and weakness of hand and forearm muscles and analgesia of the hand than an ulnar lesion could produce. Furthermore she had marked scoliosis and stiffness of the cervical spine. The radiograph of the latter does, I consider, show osteoarthritis to be present in that region. It is probable, therefore, that this patient sustained a lesion of her cervical cord and roots as the result of an accident in which her head was caught in a door. I would recommend lateral and oblique views of her cervical spine to demonstrate the condition of the disc spaces and the intervertebral foramina. It may even be that the condition of her scapula is a "trophic" necrosis secondary to her neurological condition, or ischaemic through a damage to, and thrombosis in, her transverse cervical artery occurring at the same time as her other injuries.

**Fractured Lunate Bone Replaced by Plastic Cast.**—E. L. TRICKEY, M.B., B.S. (for St. J. D. BUXTON, F.R.C.S.).

J. H. R., aged 41. Lorry Driver.

3.12.47: Patient first seen because of pain in left wrist following injury. X-ray shows flattening and irregular sclerosis of lunate bone (figs. 1 and 2).



FIG. 1.



FIG. 2.

FIGS. 1 and 2.—A.P. and lateral radiographs, 3.12.47.

21.5.48: Left carpal lunate bone removed. Stent mould taken of cavity left in proximal row of carpus. From stent mould a plastic cast was made of methyl methacrylate.

paravertebral abscesses are present. Conversely, these symptoms and atypical pleurisy should lead the physician to search for a focus of disease in the spine in a case where there is otherwise no reason to suspect its presence.

(2) The immediate outlook is not bad in cases in which rupture into the pleural cavity occurs

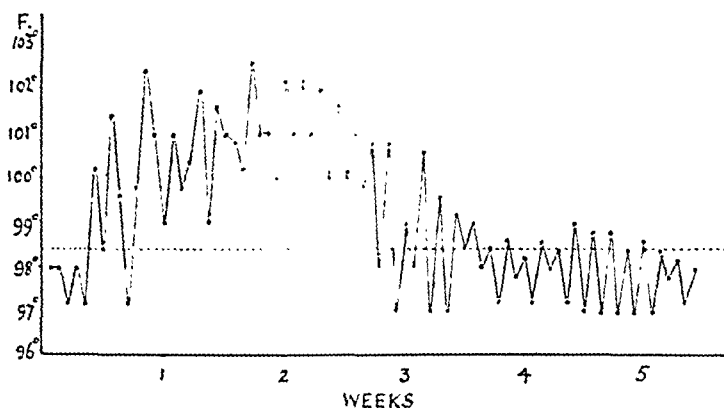


FIG. 5.—Temperature chart.

while the patient is being treated in recumbency for the spinal disease. Repeated aspiration is of great value.

(3) Patients in whom the diagnosis of spinal caries has been missed, or who have reached the ambulant stage of treatment when rupture has occurred, appear to do badly in spite of surgical drainage (laminectomy, costo-transversectomy).

(4) Rupture into a bronchus leads to secondary infection and the results of surgical drainage are not encouraging.

(5) The occurrence of rupture of a paravertebral abscess in a case in which compression paraplegia is already present is of very grave prognostic significance.

#### REFERENCES

- BRAND, M. A. (1939) *Amer. Rev. Tuberc.*, 40, 473.  
 BROOKS, W. D. W. (1942) *Brit. J. Tuberc.*, 36, 49.  
 EMROLAEV, A. (1939) *Probl. Tuberc.*, 9, 94.  
 IMBUCH, R. (1937) *Munch. med. Wschr.*, 85, 589.  
 DE LUCCHI, G. (1940) *G. Med. Marca Trevig.*, 1, 470.  
 SEDDON, H. J. (1936) *Proc. R. Soc. Med.*, 29, 1662.  
 SOMERVILLE, E. W., and WISHART, J. (1948) *J. Bone Jt. Surg.*, 30B, p. 327.  
 STARKIE, E. G. T. (1938) Cases shown at Tub. Assn. meeting at Oxford.

Mr. K. I. Nissen said that he doubted the diagnosis of spontaneous rupture of a tuberculous mediastinal abscess into the pleural cavity of a patient at rest. For one thing the pleura could be expected to adhere to and seal over an area of incipient rupture and so direct any further spread into the parenchyma of the lung. Again, the effusion in this case soon resolved uneventfully, whereas known cases of gross soiling of the pleural cavity did not always escape so lightly. Thus a patient with a closed tuberculous retro-mammary abscess had this opened with excessive vigour by Hilton's method; the pleura and internal mammary artery were ruptured and some pus was aspirated inwards; a tuberculous empyema gradually developed and proved fatal in four months. It was reasonable to expect that the rupture of an erosive mediastinal abscess would be followed by similar aspiration and a heavy infection.

In practice the greatest risk of such infection was from a pleural tear during costo-transversectomy. This risk was considerably increased by the wide resection of the modern lateral approach for decompression of the cord. A pleural tear was a grave error in technique and one which might prove fatal after a deceptive period prior to the development of an empyema.



Wishart, 1948. Consideration of these cases and the present one leads to the following conclusions:

(1) Dry cough and pain in the chest are common symptoms of pleural irritation in incipient rupture of a paravertebral abscess, and should be watched for in cases of spinal caries in which



FIG. 1.

FIG. 1 (20.4.48).—A.P. view of thoracic spine. Caries T.8 and 9 and long paravertebral abscess shadow.

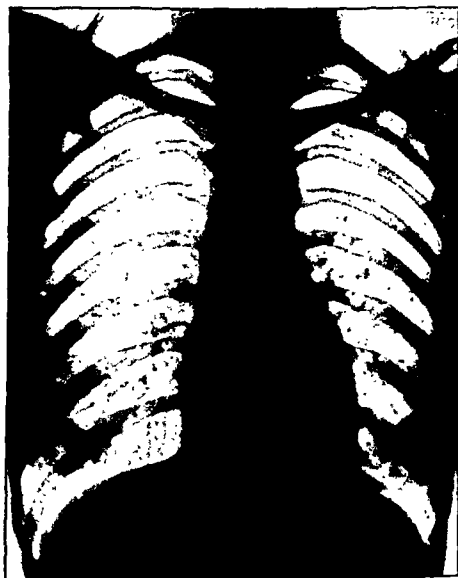


FIG. 2.

FIG. 2 (20.4.48).—A.P. view of chest; lung fields clear.



FIG. 3.

FIG. 3 (28.6.48).—A.P. view of thoracic spine. Caries T.8 and 9, disappearance of right paravertebral abscess shadow.



FIG. 4.

FIG. 4 (28.6.48).—A.P. view of chest. Right pleural effusion.

### Osteochondritis Right Talus.—E. T. BARTY, M.B., F.R.C.S.

Young, married woman, now aged 19. She sustained severe multiple injuries in a flying-bomb disaster in 1944, with no immediate reference of symptoms to the right ankle until four weeks later when she complained of some weakness. X-ray results were negative and no further trouble arose until two years later when she returned complaining of severe pains in the right ankle which now showed osteochondritis.

The ankle was explored by operation and a ragged cartilage excised, undermined edges were cut away, leaving a smooth surface. Immediate post-operative recovery was satisfactory, but symptoms recurred during her subsequent confinement which followed shortly afterwards.

Twelve weeks' immobilization in plaster was instituted, but on removal the symptoms again recurred. The question of further exploration is under consideration should physiotherapy and remedial treatment of the foot fail.



FIG. 1.—Before operation.



FIG. 2.—Recurrence of symptoms one year after operation. Treated by three months' plaster immobilization.

### Ununited Nine-Year-Old Fracture of the Mid-Shaft of The Femur.—G. J. WALLEY, F.R.C.S.

John W., aged 37. A toolmaker.

July 1939: The patient was involved in a motor cycle accident sustaining: (1) A fracture through the angle of the right side of the mandible. (2) Fracture of the mid-shaft of the right femur. (3) Fracture of the junction of the upper and middle-thirds of the right tibia.

He was admitted to another hospital, and immobilized between sandbags until 5.11.39, when he was discharged owing to Service bed requirements. At this time the union of the leg fractures was subjectively "solid", and he could cycle. He was readmitted to the same hospital 5.11.40 for open reduction and inlay bone-grafting, but only open reduction was performed, followed by four months' immobilization. Union did not occur, and he was fitted in 1941 by the same hospital with a bucket caliper.

The patient is a well-built and well-developed man of high morale. The right side of the mandible shows a fracture of the angle which is clinically and radiographically ununited. He suffers no disability from this and can eat painlessly.

### Osteogenesis Imperfecta in Father and Son.—E. T. BAILEY, M.B., F.R.C.S.

*Father.*—In this case the father, now aged 43, himself a sufferer from osteogenesis imperfecta, first came under notice while visiting his son. He was anxious that the boy should not suffer by neglect as he himself had done, with the result that he was deformed to such an extent that he walked on his knees only, with short sticks and could neither read nor write.

It was felt that, despite these handicaps, he was an intelligent, active man, for whom adequate resettlement could be made. The Public Assistance authorities, on whom he was dependent, refused to provide calipers for him to walk. The help of the Ministry of Labour was invoked with the request to provide calipers on the same terms as artificial limbs for amputation cases. Administrative objection that the patient still had his legs was overruled by representations to the Ministry of Labour Headquarters, who not only provided him with calipers at Roehampton.



FIGS. 1 and 2.—C. F. (Senior).

Femur and tibia showing malunion and severe bowing.



FIGS. 3 and 4.—C. F. (Junior).

FIG. 3.—Femur showing multiple fractures. FIG. 4.—Length and position controlled by Thomas's splint with fixed strapping extension.

but installed equipment for him to earn his living as a boot and shoe repairer, rendering him economically independent. His educational deficiencies are covered by instruction given together with his own son.

*Son.*—Boy aged 9 years.

*History* of multiple fractures of the upper and lower limbs, commencing with a fracture of the tibia at 6 months old. When he was first seen at the age of 6 years he had by then sustained fourteen fractures of the arms and legs and was admitted for a recent fracture of the right femur.

He was treated by strapping extension and subsequent walking calipers, but re-fractured whilst still in hospital on several occasions from minor causes. He was eventually discharged home wearing his calipers, but fractures continued to occur at intervals of a few weeks, necessitating hospitalization until home management of the boy was instituted satisfactorily by training the mother in the use of a fixed strapping extension with a Thomas's splint supplied to her for the purpose.

Fractures continued to occur, but were controlled adequately by this means with Out-Patient attendances for X-ray control.

**Elephantiasis Nervorum.**—PAUL MARCHAND, M.B. Witwatersrand, F.R.C.S., *late R.S.O., Royal National Orthopaedic Hospital, London.*

D. L., aged 17.

This patient has been under observation as an out-patient at the Royal National Orthopaedic Hospital since March 1945. At that time his left leg was  $1\frac{1}{2}$  in. longer than the right but there was no note of any unusual swelling.

In February 1946 he had developed an equinovarus deformity of his foot of paralytic origin. There was still no note as to any swelling of the limb. In June 1948 swelling around the left ankle was first noticed. This steadily increased and was associated with marked tenderness about the ankle (fig. 1).

*Family history.*—There was no history of any similar condition in any member of his family.

*Past illnesses.*—Nothing significant.

*General examination.*—Undernourished boy, small for his age. Carious teeth. There was widespread pigmentation of his skin, especially over the buttocks and down the left leg. This was a typical "café-au-lait" type. There were no nodularities in the skin. The left leg was held in equinovarus and there was a moderate degree of pes cavus. There was diffuse swelling of the soft parts, extending from mid-calf to the ankle, which did not pit on pressure. There was very marked tenderness behind the medial malleolus. The external popliteal nerve could be felt to be grossly enlarged as it wound around the head of the fibula.

On these clinical findings a diagnosis of elephantiasis nervorum was made.

X-ray showed diffuse areas of decalcification and irregularity in the bone structure extending upwards to L.2 (most marked in upper third of left femur) (fig. 2). Paralysis and pain were taken to be highly suggestive of sarcomatous change and on this account it was thought advisable to amputate the limb. This was performed by Mr. J. I. P. James on 25.10.48, a below-knee amputation being performed, the anterior tibial and external popliteal nerves being removed through a separate incision. The other nerves were pulled down and divided as high as possible. The limb was subsequently dissected and the following are the main points of interest (fig. 3):

(1) Gross enlargement of the cutaneous nerves especially the musculocutaneous and the sural nerves.

(2) Parallel enlargement of the twigs of these nerves which approach the size of the normal sural.

(3) Enormous enlargement of the deeper nerves—the anterior tibial, the posterior tibial and the peroneal.

(4) Gross fusiform swelling of the posterior tibial nerve behind the medial malleolus. The swelling is localized to a part of the enlarged nerve.

There is no evidence of extension and the mass remains completely localized.

(NOTE.—This was the site of tenderness on clinical examination, and at that time it was taken as presumptive evidence that the condition had undergone malignant change.)

(5) Thickening of the periosteum is shown over the subcutaneous portion of the

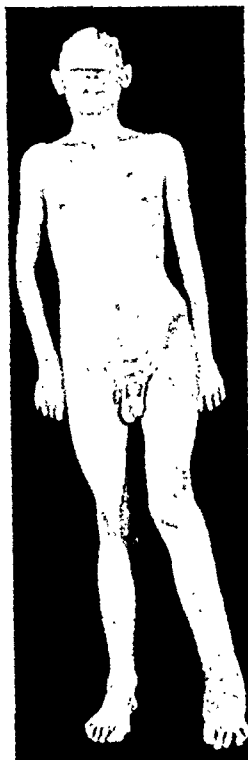


FIG. 1.—Patient D. L., showing elephantiasis and the lengthening of the left lower limb. Note the paralytic equinovarus.

*Right leg:* There is  $4\frac{1}{2}$  in. real shortening with multiple scarring of the thigh. Hip-joint movement is virtually full. Clinically and radiographically there is non-union of the femoral fracture. The patient can lift this leg up to 90 degrees quite straight. He can stand on the right leg, unsupported, for periods of minutes on end. The range of right knee movement is from 180 degrees to 160 degrees and there is no effusion or pain.

The fracture of the right tibia is clinically and radiographically united.

The patient was shown: (a) as a curiosity, in that he could stand well on an ununited fracture of the femur. (b) For the advice of the Section as to the future management of his condition.



FIG. 1.



FIG. 2.



FIG. 3.

FIG. 1 (20.10.48).—Lateral radiograph of the united tibial fracture, Rt. FIG. 2.—Lateral radiograph of the ununited femoral fracture, Rt. FIG. 3.—Non-union of the fracture of the angle, Rt. side of the mandible.



FIG. 4.



FIG. 5.



FIG. 6.

FIG. 4 (19.10.48).—Weight bearing on the Rt. leg. FIG. 5.—Straight leg raising Rt. leg. FIG. 6.—Demonstrating the angulation possible at the ununited Rt. femoral fracture site.

# PROCEEDINGS *of the* ROYAL SOCIETY OF MEDICINE

ISSUED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE

HONORARY EDITORS

ERIC A. CROOK      E. R. CULLINAN

EDITOR

J. M. BROWNE KUTSCHBACH

|                                           |                                 |
|-------------------------------------------|---------------------------------|
| G. S. W. ORGANE (Anæsthetics)             | F. T. RIDLEY (Ophthalmology)    |
| J. S. RICHARDSON (Clinical)               | H. L.-C. WOOD (Orthopædics)     |
| J. B. BROOKSBY (Comparative Medicine)     | C. S. HALLPIKE (Otolary)        |
| E. W. PROSSER THOMAS (Dermatology)        | A. G. SIGNY (Pædiatrics)        |
| E. F. SCOWEN (Endocrinology)              | F. R. SELBIE (Pathology)        |
| ALLAN McFARLAN (Epidem. & State Med.)     | M. B. RAY (Physical Medicine)   |
| A. C. WHITE (Exper. Med. & Therap.)       | O. V. LLOYD-DAVIES (Proctology) |
| I. E. McCracken (History of Medicine)     | DENIS HILL (Psychiatry)         |
| W. A. MILL (Laryngology)                  | F. CAMPBELL GOLDING (Radiology) |
| MAURICE DAVIDSON (Medicine)               | CHARLES DONALD (Surgery)        |
| J. St. C. ELKINGTON (Neurology)           | G. M. FINDLAY (United Services) |
| LESLIE WILLIAMS (Obstetrics & Gynæcology) | A. CLIFFORD MORSON (Urology)    |
| B. W. FICKLING (Odontology)               |                                 |

SECRETARY OF THE ROYAL SOCIETY OF MEDICINE

G. R. EDWARDS

tibia. This is almost  $\frac{1}{4}$  in. in thickness. Sections show fibrosis but otherwise no abnormality.

*Histological report* (Dr. C. H. Lack, R.N.O. Hospital).—*Tumour of Nerve in Amputated Leg:* This tissue is made up of bundles of nerve fibres with very little adventitial fibrous tissue. The appearances are those of a plexiform neuroma. The nerves within the bundles are all atrophic; they stain poorly while their fibrous sheaths are thickened and show up clearly. There is no sign of sarcomatous change.

*Comment.*—The condition was very widespread, affecting almost every nerve in the limb. It is interesting to note that the elephantiasis, which was confined



FIG. 2.



FIG. 3.

FIG. 2.—X-ray of pelvis to show localized areas of decalcification and the general atrophy of the left femur.

FIG. 3.—Specimen: Note the tumour of the posterior tibial nerve as it passes behind the medial malleolus. The posterior tibial nerve itself is enormously enlarged.

to the region of the ankle-joint, corresponded to the tumour area in the posterior tibial nerve. In this case the elephantiasis could have been accounted for purely by the swelling in the posterior tibial nerve combined with the periosteal thickening and the enlargement of the other nerves in that region. The two signs which had been taken as highly suggestive of malignancy do not appear to have been confirmed, notably the severe pain felt behind the medial malleolus and the paralysis of the external popliteal nerve.

# PROCEEDINGS

## OF THE

# ROYAL SOCIETY OF MEDICINE

Vol. XLII No. 6 June 1949

## CONTENTS

|                                                                                                                                                         | Whole<br>Proceedings<br>Page |
|---------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|
| <b>Section of Obstetrics and Gynaecology</b>                                                                                                            |                              |
| <i>January 21, 1949</i>                                                                                                                                 |                              |
| DISCUSSION ON THE PATHOLOGICAL FEATURES OF CORTICAL NECROSIS OF THE KIDNEY AND ALLIED CONDITIONS ASSOCIATED WITH PREGNANCY .. .. .                      | 375                          |
| <i>February 18, 1949</i>                                                                                                                                |                              |
| Vault-Suspension.—By HUMPHREY G. E. ARTHUR, M.D., F.R.C.S., M.R.C.O.G. ..                                                                               | 388                          |
| Some Aspects of Non-Gonococcal Infections of the Genital Tract. [Abridged]. By A. H. HARKNESS, M.R.C.S., L.R.C.P. .. .. .                               | 390                          |
| <b>Section of Odontology</b>                                                                                                                            |                              |
| The Hypotheses Concerning the Aetiology of Dental Caries. By GILBERT J. PARFITT, M.R.C.S., L.R.C.P., F.D.S. R.C.S. .. .. .                              | 393                          |
| Birth Conditions and Dental Deformities.—By LILAH M. CLINCH, L.D.S. R.C.S.I. ..                                                                         | 399                          |
| <b>Section of Epidemiology and State Medicine</b>                                                                                                       |                              |
| <i>January 3, 1949</i>                                                                                                                                  |                              |
| DISCUSSION: HOW TO WRITE A REPORT. [Abstract] .. .. .                                                                                                   | 401                          |
| <i>April 4, 1949</i>                                                                                                                                    |                              |
| DISCUSSION ON IMMUNITY RESPONSES IN THE YOUNG WITH SPECIAL REFERENCE TO DIPHTHERIA .. .. .                                                              | 402                          |
| <b>Section of the History of Medicine</b>                                                                                                               |                              |
| <i>November 3, 1948</i>                                                                                                                                 |                              |
| Antonio de Gimbernat, 1734-1816.—By N. M. MATHESON, F.R.C.S. .. .. .                                                                                    | 407                          |
| <i>January 5, 1949</i>                                                                                                                                  |                              |
| Eighteenth Century Medical Care: A Study of Roxburghshire.—By IAN E. MCCracken, M.D., B.Hy., D.P.H. .. .. .                                             | 410                          |
| <b>Section of Physical Medicine</b>                                                                                                                     |                              |
| DISCUSSION ON MANIPULATIVE TREATMENT .. .. .                                                                                                            | 417                          |
| <b>Section of Otolaryngology</b>                                                                                                                        |                              |
| Extensions of the Tympanic Cavity. [Summary].—By Professor VICTOR LAMBERT, F.R.C.S. Ed. .. .. .                                                         | 421                          |
| The Aetiology of Swimmers' Exostoses of the External Auditory Canals and of Associated Changes in Hearing.—By W. STIRK ADAMS, F.R.C.S. [Résumé] .. .. . | 424                          |
| Demonstration of the Human Labyrinth and its Related Structures in Perspex.—By OLIVER GRAY, M.B.E., B.A., M.B., Ch.B. .. .. .                           | 425                          |
| <b>Section of Orthopaedics</b>                                                                                                                          |                              |
| The Practical Value of Peripheral Nerve Repair.—President's Address by H. J. SEDDON, M.A., D.M., F.R.C.S. .. .. .                                       | 427                          |
| <b>Section of Surgery</b>                                                                                                                               |                              |
| <i>January 5, 1949</i>                                                                                                                                  |                              |
| List of Specimens shown .. .. .                                                                                                                         | 437                          |
| <i>March 2, 1949</i>                                                                                                                                    |                              |
| DISCUSSION ON THE SURGERY OF PORTAL HYPERTENSION .. .. .                                                                                                | 437                          |

(Continued on next page)





NEW PRESENTATION  
25 mg. Glossettes.

REDUCTION IN PRICE  
of 5 mg. Glossettes.

# METHYLTESTOSTERONE

GLOSSO-STERANDRYL 25 mg. (ROUSSEL)

SUBLINGUAL ADMINISTRATION

NOW IN TWO STRENGTHS

5 mg. and 25 mg.

## ADVANTAGES OF THE 25 mg. GLOSSETTES

**Small Doses :** One 25 mg. Glossette per day, instead of five 5 mg. obviates the inconvenience of having to retain them in the mouth for a period five times as long.

**High Doses :** Until now, there has been no convenient method for the sublingual administration of high doses of male hormone. This is now possible using repeated daily administration of the 25 mg. Glossettes.

**IN THE MALE :** Hypogonitalism, Male climacteric, Senility.

**IN THE FEMALE :** Metrorrhagia, Premenopausal disorders.

5 mg. Glossettes : 20...12/9, 100...57/6, 500...266/-

25 mg. Glossettes : 10...28/-, 20...56/-, 100...252/- 250...610/-



ROUSSEL LABORATORIES LIMITED  
95 Great Portland Street, London, W.1. LAN 3744

## Section of Obstetrics and Gynæcology

President—Professor HILDA N. LLOYD, F.R.C.S., F.R.C.O.G.

[January 21, 1948]

### DISCUSSION ON THE PATHOLOGICAL FEATURES OF CORTICAL NECROSIS OF THE KIDNEY AND ALLIED CONDITIONS ASSOCIATED WITH PREGNANCY

Professor James Young: The present discussion is concerned with those acute states in relation to pregnancy which have as their dominant features anuria or severe oliguria, increasing azotæmia and uræmia. The result is death usually within seven to twelve days or, alternatively, increasing diuresis associated typically with a rapid declension in the uræmia and ending, it would seem in the ordinary case, in complete recovery.

This clinical sequence is found:

(1) In cases of *accidental hæmorrhage*. This is the most common association and the anuric state is more frequent in "concealed" than in so-called "revealed" cases. In a study of 79 consecutive cases of accidental hæmorrhage, 59 of which were revealed and 20 concealed, we found the sequence restricted to the latter group. In this it occurred five times or in 25%.

(2) In *obstructed labour* especially where there has been long-standing compression trauma of the soft passages (Young and McMichael, 1941).

In concealed hæmorrhage and in puerperal trauma the sequence is usually preceded by clinical shock which may be severe.

In many instances the renal lesion is markedly selective. In the case of traumatic anuria, however, the renal failure may be associated with a massive degenerative lesion of the liver and jaundice, the degeneration involving especially the mid-zonal and central regions of the lobule. But whilst the renal lesion may be quite typical it would seem that the fatigue of the prolonged labour, severe nutritional inanition and inept anæsthesia have often contributed to the production of a complex pathology.

(3) In rare cases of *eclampsia*. It is well known that eclampsia may occur in association with concealed accidental hæmorrhage and the anuric syndrome. The sequence may rarely occur in eclamptic cases without concealed hæmorrhage.

(4) It may very rarely occur during the course of a pregnancy which seems otherwise apparently normal (Kellar and Arnott, 1933).

(5) To complete the list we have, finally, to note a group of conditions in which the anuric sequence is merely incidental to pregnancy, e.g. incompatible transfusion, after the administration of sulpha drugs and in association with certain infective conditions in the puerperium, especially that due to *Clostridium welchii*.

Of proximate ætiology we have little or no knowledge. It has been suggested that the kidney lesion is due to anoxia from circulatory collapse following on the shock of the utero-placental hæmorrhage. But in other obstetrical conditions apt to be associated with as severe or more severe hæmorrhagic shock, e.g. placenta prævia and puerperal hæmorrhage, the sequence is unknown. Thus in 59 consecutive cases of severe hæmorrhage at childbirth necessitating blood transfusion and including 37 cases of post-partum bleeding, 12 cases of placenta prævia and 10 cases of concealed accidental hæmorrhage, the anuric sequence occurred in 5 or 50% of the last group and in none of the others. Moreover, all degrees of the anuric phenomenon are clinically recognizable and in the milder cases there has often been no evidence of shock whatever. Moreover, even complete suppression of urine can occur in a case without any shock.

It has sometimes been assumed that the total sequence—accidental hæmorrhage—anuria—azotæmia—is merely one manifestation of pregnancy toxæmia. This view is supported by the frequency with which it occurs as the final and critical climax in a toxæmic patient. But there is no doubt that the anuric and uræmic sequence postdates the acute utero-placental lesion. Moreover, as I have shown, there may be no evidence of antecedent toxæmia. The patient may have the acute pain in the abdomen associated with the retroplacental bleeding and only after an interval of hours—the oliguria, albuminuria, &c., develop. Unless we revive such speculative possibilities as occult toxæmia, which in the past have been of meagre service in this class of discussion, we cannot evade the conclusion that it is the utero-placental lesion which precipitates the kidney damage.

## Section of Ophthalmology

February 11, 1949

The Retro-orbital Tissues as a Site of Outflow of Cerebrospinal Fluid.—By E. J.

FIELD, M.D., M.S., and J. B. BRIERLEY, M.D. . . . . 447

March 10, 1949

DISCUSSION ON OPHTHALMIC PHOTOGRAPHY. . . . . 451

(N.B.—The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.)

All communications concerning Editorial Business should be addressed to  
THE HONORARY EDITORS, 1, WIMPOLE STREET, LONDON, W.1

Applications for advertisement space in the "Proceedings" should be made to the Society's official advertising agents,  
Messrs. C. Mitchell & Co. Ltd., Mitchell House, 1 and 2, Snow Hill, London, E.C.1.

Copies of the whole *Proceedings* may be purchased through any bookseller. Prices are as follows:—

|                                                                                              |                           |
|----------------------------------------------------------------------------------------------|---------------------------|
| Single copies                                                                                | 10s. 6d. each, post free. |
| Annual subscription, covering 12 monthly issues and annual index                             | £6 6s. 0d.                |
| Reprints of Sectional parts may be obtained direct from the Society. Prices are as follows:— |                           |
| Single copies                                                                                | 3s. 6d. each, post free.  |
| Annual subscription                                                                          | 15s. 0d.                  |

Fellows and Members of the Royal Society of Medicine are asked to apply direct to the Society for any copies of the *Proceedings* they may require, whether whole or Sectional, in addition to those they receive *gratis*. Prices are as follows:—

|                                                      |                          |
|------------------------------------------------------|--------------------------|
| Whole <i>Proceedings</i> :                           |                          |
| Single copies                                        | 7s. 6d. each, post free. |
| Complete volume (12 monthly issues and annual index) | £5 0s. 0d.               |
| Sectional <i>Proceedings</i> :                       |                          |
| Single copies                                        | 3s. 0d. each, post free. |
| Annual subscription                                  | 10s. 0d.                 |

## Publication Rules.

**Copyright:** The Society holds the copyright of all matter accepted for publication in the *Proceedings*. Requests for subsequent publication elsewhere should be made to the Honorary Editors. All papers, &c., presented at meetings (other than those which have been previously published) are held to be subject to the Society's copyright until a decision in regard to their publication has been made.

**Digests:** Requests for permission to make Digests from the *Proceedings* should be addressed to the Honorary Editors.

**Manuscripts** should be concise and *carefully revised for press*. They must be top copies, typewritten in double spacing, with the author's name, degrees and address on the first page. A carbon copy should be retained by the author.

The text must contain references to all tables and illustrations; these should be numbered and packed separately.

Dosages and other measurements should be given in metric units.

**References:** The Harvard system should be followed, i.e. each work should be cited in the text by the author's name and date of publication, and at the end of the paper a list should be given in alphabetical order according to the authors' names. Names of journals should be abbreviated in accordance with the "World List of Scientific Periodicals", e.g. ATKINSON, J. (1921) *J. biol. Chem.*, 47, 134.

With the title of a book the name of the publisher and the place of publication should be given.

**Illustrations** should be numbered consecutively and the top clearly marked. They must be suitable for direct photographic reproduction.

Photographs should be glossy prints. *No negatives or slides will be accepted*. The important feature of each photograph should be indicated, preferably by pencil lines on the back.

All numerals, &c., appearing on diagrams should be large and bold to allow of reduction in size.

**Blocks** used for the illustration of articles in the *Proceedings* will be presented to authors shortly after each volume is concluded.

**Reprints** may be obtained from the Society's printers, Messrs. Staples Press Limited, 83-91, Great Titchfield Street, London, W.1.

between lower nephron nephrosis and cortical necrosis have already been emphasized by Bywaters (1948) although he did not deal specifically with anuria in pregnancy.

It is convenient first to describe the morbid anatomy in a typical case of lower nephron nephrosis.

A coloured woman, aged 21, was admitted to the London Hospital in November 1948, three days after an illegal abortion had been performed, having given a false history. She was 15 weeks' pregnant. Surgical evacuation of the uterus was performed shortly after admission. At this time she was not acutely ill and her condition did not give rise to anxiety until a few minutes before her death a week later, except that she had a moderate oliguria. Soon after admission one specimen of urine was reported to contain blood but this was not examined by the laboratory (it may well have contained pigment). A catheter specimen of urine yielded pus and *Bact. coli*. On admission her blood haemoglobin was 57%. The blood urea was 102 mg. % on the day of her death. Culture of a cervical swab yielded *Clostridium welchii* but at no time was there any indication of septicæmia: her pulse was never above 104 and she did not appear severely ill. However, a week after admission she suddenly became distressed, dyspnoic, with cyanosis of the lips and pallor of the extremities, her pulse was rapid and thready and she died within a few minutes. It is perhaps important to note that she had been receiving potassium citrate 60 grains four-hourly for three days because of her urinary infection.

At necropsy the uterus was slightly enlarged with a smooth glistening serosa and two areas of necrosis in the mucosa, the larger of these being probably the placental site. Small pieces of ant-mortem thrombus were present in the uterine veins below the necrotic areas, the myometrium here being congested but not necrotic. The kidneys were enlarged (14½ oz.), and smooth with a pinkish-grey, very oedematous cortex; the medulla congested and in places showing greenish radial streaks on the cut surface. There was a unilateral pyelitis and marked cystitis.

On microscopic examination of the kidneys, the presence of pyelitis on one side is confirmed, otherwise similar changes are present in both. The glomeruli are normal. The epithelium of the first convoluted tubules and of the descending limbs of Henle show slight degeneration only. The epithelium of the ascending limbs of Henle and of the second convoluted tubules has undergone severe necrosis in some areas, while in others marked regeneration is evident (fig. 1). These changes in the epithelium are associated with copper-coloured ribbon and granular casts in the lumina of the tubules, and similar casts are present in many collecting tubules. These casts give a positive benzidine reaction and are therefore presumably composed of a derivative of haemoglobin or myohaemoglobin. The periphery of some casts is infiltrated with polymorphonuclear leucocytes; about others there are macrophages and occasionally foreign body giant cells have formed around granules of the pigment. A few tubules contain hyaline casts. In the intermediate zone there are foci of infiltration with histiocytes, lymphocytes and eosinophils in the interstitial tissue. Some of these are associated with tubulo-venous fistulae, others with extrusion of the hyaline type of cast into the interstitial tissue through necrotic or incompletely regenerated epithelium of the lower nephron (figs. 2 and 3). There is congestion of the vasa recta, a few of which are filled with lymphocytes and other mononuclear cells suggesting that in these few at any rate the circulation is sluggish. The oedema of the interstitial tissue which was such a marked feature to the naked eye is confirmed.

From the histological material collected at the London Hospital during the last twenty years I have examined material from three similar cases. In none was the period of survival after abortion so long, and in none was the regeneration of epithelium around the granular casts so marked. The essential features of lower nephron nephrosis were present, however, in all.

The presence of pigment casts in the tubules of the kidney in fatal cases of anuria complicating septic abortions was first described by Bratton in 1941. Subsequently it was recognized that the histological picture was similar to that seen in the crush syndrome and incompatible blood-transfusion. To me the aetiology is still uncertain. Professor Young (1942a, b, 1947) has stressed its association with utero-placental damage, but in the case that I have described in some detail, the degree of damage to the uterus was slight. So far as I am aware the exact nature of the pigment in the tubules is still uncertain and careful spectroscopic examination of the urine in future cases is indicated. I wish to emphasize that in this condition of lower nephron nephrosis the damage is essentially to the epithelium of the second convoluted tubules and of the ascending limbs of Henle, the glomeruli and the first convoluted tubules being virtually normal.

It may be asked whether such a disturbance of the kidney complicates pregnancy apart from septic abortion. Practically all writers on the pathology of eclampsia have described, in a small percentage of cases, the presence of granular casts containing a haemoglobin derivative in the tubules of the medulla and in a few tubules of the cortex. I have examined necropsy material from 17 cases of eclampsia that died at the London Hospital between 1920 and 1940 and have found these pigment casts in the second convoluted tubules, the ascending limbs of Henle and in collecting tubules in three. Associated with the casts there was evidence of necrosis and some regeneration of the tubular epithelium, but not of the same intensity as that seen in the case which I described first. In two of these three cases there was a clinical history of severe oliguria; observations in this respect are not available for the third. Thirty years ago it may be recalled Clifford White, writing in the *Proceedings* of this Section of the Society, described two cases of eclampsia complicated by

It is when we come to the consideration of the pathology of the kidney that we find perhaps the most intriguing circumstances surrounding the whole subject. And here I shall confine my remarks to the findings in cases of concealed accidental hæmorrhage about which we have more precise information. We now know that, despite the uniformity of the clinical sequence and of the utero-placental pathology in such cases, two quite different types of lesion are found in the kidney. In the first place we have bilateral cortical necrosis. This is the lesion which in the past has been more particularly identified with the anuric sequence, but we now believe that it is the rarer of the two lesions. In the second place we have the lower nephron lesion affecting the second convoluted and collecting tubules, associated with degeneration of the epithelium and, frequently but not invariably, with the deposit of crystals of blood pigment, often in considerable amount, in the tubules.

The lower nephron lesion is similar to that described by Bywaters and Dible (1942) in the kidneys obtained from fatal cases of anuria after crushing injuries sustained during bombing raids. Bratton (1941) first described this kidney lesion in obstetrical anuria and Dible and I found it in three of four kidneys from cases of anuria following concealed accidental hæmorrhage made available to us for study (Young, 1942).

The resemblance between the kidney lesion of obstetrical anuria and that found in crush cases naturally raises the possibility of a basic similarity in genesis. It seems unlikely that in either condition tubal blockage by pigment casts is an essential factor. Bywaters and Dible (1942) have shown that the kidneys obtained after early death in crush cases may exhibit no blood casts. Similarly in obstetrical anuria pigment casts are not always found (Young, 1942). As in both conditions there is massive tissue damage of muscle in the anuria following crushing injuries and of placenta in concealed accidental hæmorrhage, it is conceivable that toxic metabolites of tissue origin play an essential part. Eggleton (1944) has given some experimental evidence for this concept in the case of surgical anuria. Finally the investigations of Trueta and his co-workers (Trueta *et al.*, 1946) on the renal circulation point to a possible explanation of the striking duality of the kidney lesion seen especially in obstetrical anuria.

In the anuria of the crush kidney recovery can be expected in a considerable proportion of cases under appropriate treatment. We know that the majority of cases of obstetrical anuria following accidental hæmorrhage recover and we may assume that the lesion in these cases is more likely to be of the lower nephron type and less likely to be cortical in its distribution.

Those who follow me in the discussion are more able than I am to deal with questions of ætiology and pathology. But as an obstetrician I would remind you that the kidney pathology in these cases may have a special relevance in relation to the genesis of pregnancy toxæmia. I have referred to the by no means uncommon occurrence of eclampsia with or without the anuric sequence in cases of concealed accidental hæmorrhage. Further it has long been known that blood pigment casts are relatively common, with or without tubular degeneration, in the eclamptic kidney. Schmorl (1893) first described their occurrence and Fahr (1924) found hæmatin casts in the tubules in 18 out of 33 fatal cases of eclampsia. In this country Dunn and Baird (1933) found such casts in the kidneys in 3 out of 10 cases of eclampsia.

The significance of these findings is not easy to assess. It is clear that they do not constitute more than an occasional occurrence and even in the kidney of an eclamptic case dying from the anuric sequence the pigment casts may be absent.

#### REFERENCES

- BRATTON, A. B. (1941) *Lancet* (i), 345.  
 BYWATERS, E. G. L., and DIBLE, J. H. (1942) *J. Path. Bact.*, 54, 111.  
 DUNN, J. S., and BAIRD, D. (1933) *J. Path. Bact.*, 37, 291.  
 EGGLETON, M. G. (1944) *Lancet* (ii), 208.  
 FAHR, T. (1924) Article in *Die Eklampsie* (Hinselmann, H.), Bonn, 252.  
 KELLAR, R. J., and ARNOTT, W. M. (1933) *Trans. Edinb. obstetr. Soc.*, 53, 101.  
 SCHMORL, G. (1893) *Path.-Anat. Untersuchungen über Puerperal-Eklampsie*. Leipzig.  
 TRUETA, J., BARCLAY, A. E., DANIEL, P., FRANKLIN, K. J., and PRICHARD, M. M. L. (1946) *Lancet* (ii), 237.  
 YOUNG, J. (1942) *Brit. med. J.* (ii), 715.  
 —, and MCMICHAEL, J. (1941) *Brit. med. J.* (ii), 887.

**Dr. J. F. Smith:** I propose to describe briefly the morbid anatomy of the kidney in septic abortion complicated by oliguria, which has been called Lower Nephron Nephrosis (or, alternatively, Pigment Nephrosis), and to discuss its relationship to Symmetrical Cortical Necrosis. In 1947 Humphrey and Avery Jones suggested that the pathological process in the oliguria of septic abortion was probably "that whose end result was found in persons dying with symmetrical renal cortical necrosis". To me there are difficulties in accepting this view as the histology of the kidney in the two conditions is not the same. The differences

that condition are terminal events. It is highly improbable that he was able to examine more than the cortex in these cases and, from the data available, I consider that they belong to the same group as my three cases of eczempia with some degree of pigment nephrosis.

The histological picture in symmetrical cortical necrosis is in fact very different. Concealed accidental haemorrhage in the latter part of pregnancy is often an antecedent event in typical cases. The necrosis is usually massive, affecting the whole of the cortex of both kidneys except a thin subcapsular zone and a narrow zone adjacent to the medulla which are unaffected. It is often a coagulative and necrotic necrosis with a haemorrhagic border associated with thrombosis in afferent arterioles and in interlobular arteries (fig. 4). In the haemorrhagic border some glomeruli are distended with blood cells, and occasional capillary loops contain fibrin thrombi. It has been recorded by Shaw Dunn and Montgomery (1941) that the whole of the necrotic area may have this haemorrhagic appearance in early cases. These are relevant to their theory that the necrosis is due to a stasis and thrombosis within glomerular capillaries which spreads back to involve interlobular arteries. De Navasquez (1938) considered that the necrosis was due to stasis in the glomerular capillaries, afferent arterioles and interlobular arteries secondary to a necrosis of the latter. There are other views as to the mechanism of the arrest of circulation but practically all are agreed that the necrosis is a manifestation of ischaemia. I wish to emphasize that the effect of this ischaemia is to cause necrosis of all elements of the cortex, glomeruli and all convoluted tubules; and to spare the medulla. This differs profoundly from the necrosis in the kidney of septic abortion which involves a definite segment of many individual nephrons.

In connexion with the sparing of the medulla in cortical necrosis it is of interest to recall the statement of Shaw Dunn and Montgomery (1941): "Arrest of circulation is incomplete in proximal parts of interlobular arteries owing to easier escape of blood through deep glomeruli whose efferents pass by short routes direct to the medulla and not to the cortical rete."

In addition to the typical case in which cortical necrosis is massive, occasional examples of patchy cortical necrosis occur in which areas of necrotic first and second convoluted tubules are anatomically related to glomeruli whose capillaries are distended with blood, suggesting stasis therein, or in which fibrin thrombi have formed in some capillary loops. At the borders of such necrotic areas some tubules show evidence of regeneration, and others hyaline droplet change (fig. 5). In between the necrotic areas some glomeruli and

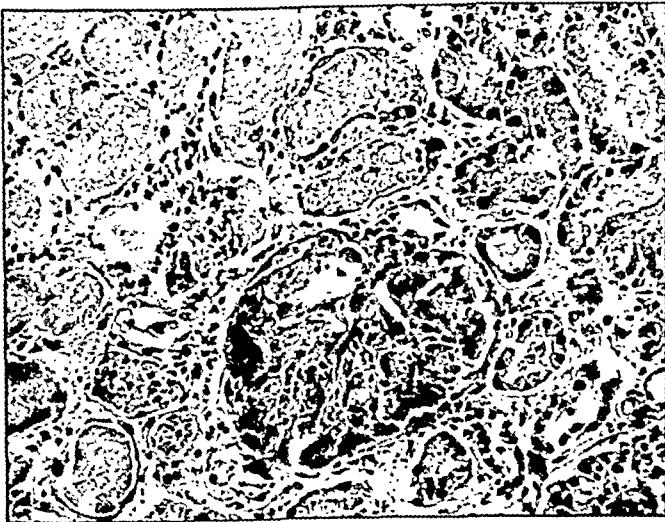


FIG. 5.—Patchy cortical necrosis associated with thrombosis in a congested glomerular tuft. Tubules above and to left of glomerulus are necrotic, those immediately above show regeneration, those to right almost normal. Haematoxylin and eosin.  $\times 185$ .

tubules are normal. In material from one such case associated with pregnancy I found that occasional tubules of the medulla contained pigment casts, which were probably derived from necrotic red cells in distended glomeruli. However, the predominating pathological factor appeared to be an uneven cortical ischaemia producing patchy necrosis of all elements of the cortex and not selective necrosis of the lower nephron. Such a histological picture in

severe oliguria in which incision of the capsule of the kidney was followed by diuresis and recovery. In biopsy specimens he described dilatation of tubules, degeneration of their epithelium and the filling of some tubules with granular material, the glomeruli showing little change. There was also focal oedema and small round-cell infiltration of interstitial tissue. He raised the possibility that, if untreated, these cases might have developed into symmetrical cortical necrosis and suggested that the thrombosis and cortical necrosis in

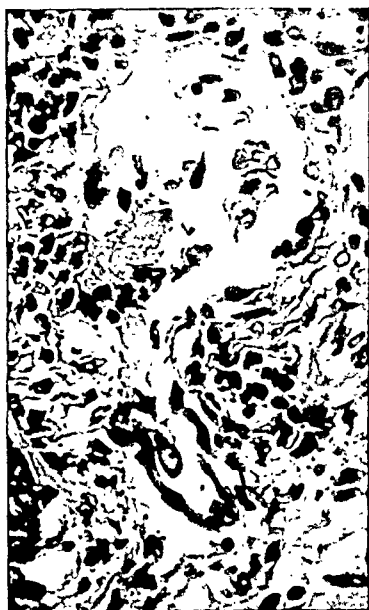


FIG. 2.—Tubulo-venous anastomosis. Hematoxylin and eosin.  $\times 325$ .



FIG. 4.—Cortex in symmetrical cortical necrosis. Glomeruli and all tubules are necrotic, there is thrombus in an afferent arteriole and one interlobular artery. Mallory's P.T.A.H.  $\times 100$ .



FIG. 1.—Cortex of kidney in lower nephron nephrosis. The casts and the associated epithelial necrosis are confined to the ascending limb of Henle and the second convoluted tubule. Hematoxylin and eosin.  $\times 118$ .



FIG. 3.—Extrusion of a hyaline cast through incompletely regenerated wall of a tubule. Hematoxylin and eosin.  $\times 325$ .

the amount of glomerular filtration surface remaining in the fully established condition. As regards the first, review of a series of cases of this condition occurring in association with concealed accidental hæmorrhage at term and in others not associated with pregnancy, shows clearly that the initial lesion demonstrable histologically is fairly uniform *glomerular capillary dilatation* (Dunn, 1941). Stasis follows and, commencing in the glomeruli, involves the blood in the afferent glomerular and intralobular arteries; thrombosis supervenes and necrosis results, involving most of the cortex in an almost continuous infarct-like lesion. The glomeruli of the boundary zone escape; the medulla is unaffected; the condition does not progress to stasis in these juxtamedullary glomeruli (or at least it quickly resolves) for being the most proximal these glomeruli have highest capillary pressure and, following stasis in the outer cortical glomeruli, the ordinary differential pressure gradient is exaggerated. A narrow subcapsular zone escapes necrosis by reason of small capsular collaterals.

These appearances can be followed from stage to stage in the experimental lesion in the rabbit, which results from the intravenous injection of staphylococcal toxin. Several years before the war I repeated the experimental work of Von Glahn and Weld (1935) and De Navasquez (1935) and confirmed the observations of Dunn (1941) regarding the initial demonstrable lesion being glomerular capillary dilatation. The conflicting views on the pathogenesis of this condition have resulted from the limited number of cases which individual authors have studied and their consequent inability to review a series sufficiently large as to include cases ranging from the earliest to the most advanced stages of the disease.

*In the human subject:* In a case fatal within forty-eight hours of the onset of anuria, the glomeruli show fairly uniform capillary dilatation; many show dilatation in extreme and there is stasis with necrosis of the related areas of cortex. At this stage, the stasis not being universal, the necrosis is not general and the lesion is patchy. In a more advanced case, in which anuria has been established for five or seven days, the necrotic zone is usually extensive and is sharply demarcated from the healthy boundary zone and medulla, and from the narrow subcapsular marginal tissue, and a leucocytic border marks the edge which is slightly hæmorrhagic and fairly vascular from attempt at collateral circulation as in ordinary renal infarction. Universal glomerular capillary dilatation is readily demonstrated in the areas of necrosis and by suitable staining can be seen, even at an advanced stage, when the patient has died after fourteen or sixteen days.

In the *experimental lesion* the genesis of the condition is more easily followed, stage by stage, since the animals can be sacrificed at intervals. The general glomerular capillary dilatation is at first segmental, at about half to one hour, and by the third hour is universal; glomeruli fill the capsule, the afferent and efferent vessels are engorged, and the intralobular arteries are dilated. A few glomeruli show capsular hæmorrhages and this accounts for the hæmaturia found in about one-quarter of the cases reported (Gibberd, 1936; Kellar and Arnott, 1933), when the period of anuria, in pregnancy cases, is preceded by severe oliguria and the scanty urine obtained on catheterization is heavily blood-stained. The glomerular capillary dilatation is often extreme and not infrequently herniation of the tuft into the first convoluted tubule occurs. A variant is aneurysmal dilatation of individual capillary loops. The onset of stasis is heralded by diapedesis of red blood cells in the walls of the afferent glomerular vessels and intralobular arteries. Thick frozen sections, photographed to show red blood cells only, demonstrate the corpuscles clearly between the muscle fibres of the vessel walls. At this stage the red cells in the lumen of the vessels show conglutination; this is soon followed by the precipitation of fibrin in the glomerular capillaries, in the wall of the afferent arteriole, and in the lumen and walls of the intralobular arteries. Stasis is now absolute and necrosis results. Resolution of stasis which was previously possible, and not infrequently occurs in the experimental animal, can no longer take place. In addition to precipitation of fibrin, fat globules appear and are deposited in the glomerular capillary loops and in the walls of the afferent and intralobular arteries. It is probable that this results from the separation of fat from the emulsified form into large aggregates. These several features, glomerular capillary dilatation, stasis, and the deposit of fibrin can be demonstrated in the necrotic zone at a very advanced stage.

To summarize: After initial segmental glomerular capillary dilatation this condition becomes universal, is followed by stasis in the tufts and is accompanied by deposition of fibrin which renders the condition irreversible. The afferent and the intralobular arteries show at first conglutination and diapedesis of red cells which is followed by stasis which becomes absolute. Stasis appears to develop from the outer cortex inwards until the deep cortical glomeruli are reached. A few of these and the juxtamedullary glomeruli escape stasis due to the higher pressure obtaining, and the circulation through these and their efferents to the medulla continues.

Although the initial histological lesion is universal glomerular capillary dilatation which proceeds to stasis, the proximate cause of the glomerular condition may be variable. It is



which a large amount of the cortex is normal would offer a pathological basis in explanation of those cases of cortical necrosis that recover.

## REFERENCES

- BRATTON, A. B. (1941) *Lancet* (i), 345.  
 BYWATERS, E. G. L. (1948) *Lancet* (i), 301.  
 DE NAVASQUEZ, S. (1938) *J. Path. Bact.*, 46, 47.  
 DUNN, J. S., and MONTGOMERY, G. L. (1941) *J. Path. Bact.*, 52, 1.  
 HUMPHREY, J. H., and JONES, F. A. (1947) *Clin. Sci.*, 6, 173.  
 WHITE, CLIFFORD (1919) *Proc. R. Soc. Med.*, 12, Sect. Obstet., 27.  
 YOUNG, J. (1942a) *J. Obstet. Gynaec.*, 49, 221.  
 — (1942b) *Brit. med. J.* (ii), 715.  
 —, and WALKER, A. H. C. (1947) *J. Obstet. Gynaec.*, 54, 196.

Professor K. J. Franklin: I imagine that the main reason why I have been asked to speak this evening is that you wish to consider if the so-called "Trueta shunt", or "Oxford shunt", or "renal shunt", can be concerned in the toxæmia of pregnancy or of its worst development, bilateral cortical necrosis.

[Professor Franklin then projected a colour film showing the shunt brought into play in rabbits, through the production of anoxia.]

My other contribution is a joint one, with my colleagues Mr. John Sophian (whose ideas started our work on eclampsia), Professor E. C. Amoroso (of the Royal Veterinary College), and Professor W. C. W. Nixon (of University College Hospital). In experimental animals, we have found that stretch (? nociceptive) stimuli to the inside of the bladder, to the inside of isolated portions of intestine, and to the inside of non-pregnant or pregnant uteri, can reflexly evoke, to a varying degree, the renal shunt. Or, in other words, the renal cortical blood flow can be diverted in part or in whole, through the incomplete adaptation of these hollow viscera to such changes of content as we attempted to impose, in acute experiments, by the introduction of saline solution at body temperatures. It may be that we should think more frequently of this triad of synergic afferent fields in relation to the toxæmia of pregnancy. Even more striking is a recent result of Professor Amoroso's. In the rabbit, the several conceptus are spaced out in the uterus, and in consequence there is room for each, as it grows, to encroach on the intervening "no-man's land". Professor Amoroso ligated the uterus on each side of each conceptus early in gestation and so caused a more natural stretch, as the conceptus grew, of the uterine muscle enclosing them. This put the shunt mechanism on such a hair-trigger basis that mere laparotomy and a touch to a conceptus region caused immediate diversion of the renal cortical blood flow. My obstetrical colleagues will cite an imposing list of circumstances in which, in the human subject, some equivalent internal stretching of the uterus can occur. Professor Amoroso will also provide examples from his sphere, and all that I would add here is that it is not inconceivable, if nociceptive end-organs are concerned, that they may be stimulated not only by stretch of the pregnant, but also by excessive spasm of the post-partum, uterus.

We have also under consideration the possible intervention of local or general anoxia in the kidney changes of pregnancy, &c., and we have begun experimental work to elucidate the matter, e.g. rabbits have had their uterine arteries ligated at their non-pregnant calibre, and have thereafter been impregnated. While we await the results, we remember that the streamlines of red arterial blood seen in the uterine veins of the cat in the early part of gestation become reduced in amount and finally disappear towards term. So any reserve provisions against local anoxia seem to become progressively less under normal conditions, and it should be interesting to see what happens with the extra strain which we have imposed.

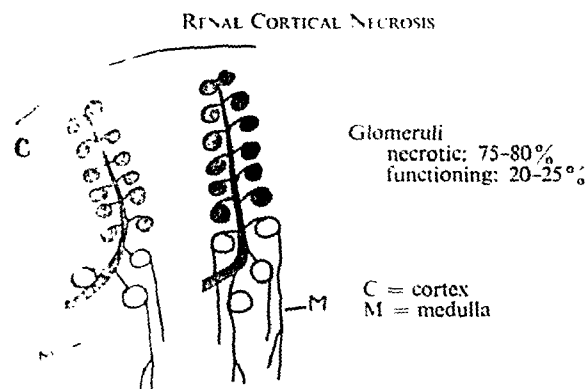
In view of our research results, obstetrical experience, and reading of the literature, my colleagues and I advance the hypothesis that toxæmia of pregnancy is, or includes, a progressively increasing tendency for the renal shunt to be brought into operation, and that fatal bilateral cortical necrosis is the maximal, irreversible result of this tendency. When the tendency to the shunt is slight, it may be regarded as a physiological reaction calculated to give the growing uterus and its contents a better blood supply at the expense of the renal cortex—we know that the kidneys receive about a sixth or a quarter of the total cardiac output at rest. When the tendency is at its most marked, we imagine that the intralobular arteries and their afferent vessels to the cortical glomeruli first constrict, but that in course of time their own nutrition is thereby affected—as shown by the observed degeneration of their tunica media, and they undergo a paralytic dilatation. But this dilatation is powerless to restore the circulation because of the simultaneous marked fall in general arterial pressure, so the relaxed vessels merely fill with blood which does not proceed further. In consequence, the intralobular arteries and the afferent vessels to the glomeruli, but not the glomeruli themselves, are found full of red blood corpuscles at autopsy.

Dr. J. F. Heggie: There are two features of renal cortical necrosis which I wish to describe and discuss. The first concerns the initial demonstrable pathological lesion and the second

volume of functioning glomeruli (juxtamedullary and a few deep cortical glomeruli) is calculated to amount to 1 c.c. and the corresponding maximum filtration surface is 0.16 sq. m., or two-fifths of the normal functioning filtration surface; but, having regard to the fact that



FIG. 3.—Early stage. Stasis is not yet declared, individual red cells are seen in the lumen. Diapedesis of red blood cells between the muscle cells in the wall is a most striking feature. (Frozen section. 20 $\mu$ . Eosin.)  $\times 400$ .



| Human subject               | glomerular capil. vol. | filtration surface |
|-----------------------------|------------------------|--------------------|
|                             | c.c.                   | sq. metres         |
| Normal                      |                        |                    |
| (a) maximum .. .. .         | 4                      | 1.56               |
| (b) usually functioning ..  | 1                      | 0.4                |
| Cortical necrosis           |                        |                    |
| (a) maximum functioning ..  | 1                      | 0.16               |
| (b) probably functioning .. | 1                      | 0.1                |

FIG. 4. Diagram—fully established cortical necrosis. The outer- and mid-cortical glomeruli from stasis proceed to thrombosis and necrosis. A few deep cortical and the juxtamedullary glomeruli carry the total normal glomerular flow over a greatly reduced filtration surface.

these glomeruli which remain functioning show fully dilated capillaries which are in intimate contact one with another, the effective filtration surface is probably no more than one-quarter (0.1 sq. m.) of the normal functioning surface in the fully established lesion. The inevitable fatality of such a state is obvious.

#### REFERENCES

- DE NAVASQUEZ, S. (1935) *J. Path. Bact.*, 41, 385.  
 DUNN, J. S., and MONTGOMERY, G. L. (1941) *J. Path. Bact.*, 52, 1.  
 GIBBERD, G. F. (1936) *J. Obstet. Gynec.*, 43, 60.  
 KELLAR, R. J., and ARNOTT, W. M. (1933) *Trans. Edinb. obstetr. Soc.*, 53, 101.  
 MILLES, G., MÜLLER, E. F., and PETERSEN, W. F. (1932) *Arch. Path.*, 13, 233.  
 VON GLAHN, W. C., and WELD, J. T. (1935) *J. exp. Med.*, 61, 1.

Dr. S. J. De Navasquez: The experimental production of symmetrical cortical necrosis of the kidneys of rabbits by means of staphylococcus toxin has enabled one to study the pathogenesis of this condition and particularly the early stages of the vascular changes, which are primarily responsible. Within three hours of the intravenous single injection of 0.1 to 0.2 c.c. of toxin per kilogram of body-weight, the peripheral cortex of the kidneys shows a patchy or diffuse congestion which on microscopic examination is seen to be due to dilatation of the intralobular arteries and afferent arterioles which are packed with red cells. This paralytic distension extends to the glomerular capillaries supplied by these vessels, leading to obstruction of the glomerular circulation.

From seven hours after the injection of toxin the renal lesion progresses to diffuse symmetrical cortical necrosis, indistinguishable morphologically from that seen in cases of pregnancy.

The lesion responsible for the paralytic dilatation of the peripheral intralobular arteries and their afferent arterioles appears to be a necrosis of the muscle of the media of these vessels, which undergoes a rapid dissolution which is complete within seven hours of the injection of toxin, no medial elements being discernible in the affected arteries after that time.

This necrosis of the media is clearly an irreversible change and will lead to complete loss of vasomotor control of the affected arteries.

to be remembered that renal cortical necrosis occurs in a variety of conditions, including childbirth and certain infections, while a few cases are recorded in which antecedent disease was absent. As in the physiological class-room experiments with the muscle-nerve preparation, in which the muscle twitches whether the stimulus applied to the nerve is chemical or physical, heat or cold, trauma or an electric current, so glomerular capillary dilatation in the renal cortex may be the ultimate response to a variety of stimuli which bring about changes in the renal circulation. In experimental renal cortical necrosis the stimulus is staphylococcal toxin which acts on the glomerular capillaries directly; the several stages of this inflammation, toxic glomerulitis, proceed to stasis and thrombosis, and result in necrosis. Vasoconstriction in the renal cortex with diversion of the circulation was demonstrated radiographically in the intact dog following severe chilling of the whole animal (Milles *et al.*, 1932). When the cold was applied for a short time only, normal return of the circulation followed cessation of the stimulus, but when the action of the cold was prolonged this was followed by marked vasodilatation in the cortex. It is also possible that other stimuli are concerned with these factors which bring about vasoconstriction of the intralobular vessels. Apart from immediate massive reflex response, as in the case of painful afferent nerve stimulus or trauma of the experiments of the Oxford workers, it is also to be

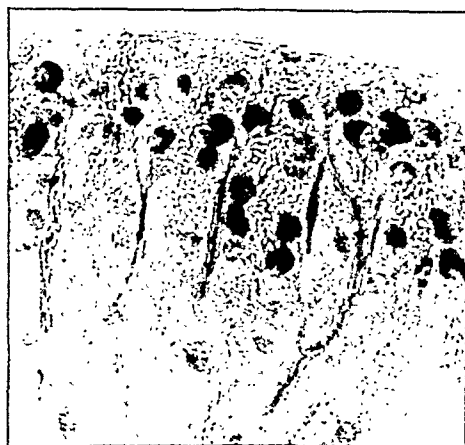


FIG. 1.

FIG. 1.—*Early stage.* The glomeruli are uniformly enlarged and engorged: intralobular and afferent arteries are dilated and diapedesis of red cells in the vessel walls is distinct. The peritubular capillary rete shows varying degrees of congestion. (Frozen section,  $20\mu$ . Unstained.)  $\times 30$ .



FIG. 2.

FIG. 2.—*Early stage.* Diapedesis in the vessel walls is more distinct. Haemorrhage into Bowman's capsule and related tubules occurs from some engorged glomeruli (hence the haematuria). Aneurysmal dilatation of glomerular capillaries is sometimes seen. (Frozen section,  $20\mu$ . Unstained.)  $\times 75$ .

considered that the vasoconstriction which follows sudden reduction in blood volume, as after haemorrhage, may be greatly exaggerated in concealed accidental haemorrhage, and that, following restoration of flow to the glomerular capillary bed, capillary dilatation is extreme so that stasis and thrombosis occur and necrosis results.

In the experimental lesion I have ascertained that the total of glomeruli operating is about 20–25 per cent. The number involved in the necrotic zones varies from 75–80 per cent. In the human subject, I have confirmed that the maximum glomerular filtration surface is 1.56 square metres, the same as the body surface of ideal man, and the maximum glomerular capillary blood volume is 4 c.c. In ordinary normal circumstances the values for the total of loops operating are probably, glomerular capillary blood volume, 1 c.c., and glomerular filtration surface, 0.4 sq. m. In bilateral renal cortical necrosis the capillary

(2) *Lower nephron nephrosis*.—Cases with this pathology have been described following concealed accidental hemorrhage, traumatic delivery, septic abortion, and blood transfusion. The clinical sequence of events is very like that of cortical necrosis, for an initial secretion of blood-stained concentrated urine, containing hyaline, granular and pigmented casts is replaced by the daily secretion of a small amount of very dilute urine until the patient dies, while the blood-urea and potassium level gradually rise. Often, however, these patients are severely ill throughout the anuric period, for sepsis and pyrexia, persistent vomiting, severe anemia, mental confusion and diarrhoea are common. And treatment with blood transfusions and sulphonamides are not uncommon measures which in themselves may precipitate suppression of urine. Altogether one gets the impression that these patients die rather from general causes than from pure toxic uræmia although, undoubtedly, suppression of urine is an important additional factor in bringing about a fatal issue.

The pathological features in this syndrome are strikingly different from those of cortical necrosis. This time the renal cortex is pale and ischemic, and the medulla is engorged; the glomeruli are living and have a healthy appearance and the characteristic lesion is in the second convoluted and collecting tubules in them the epithelium shows various stages of damage, necrosis and desquamation; and the lumina contain pigmented ribbon casts, while sometimes blood vessels near to them appear to have ruptured into them. In the later stages reparative processes can be demonstrated in the tubular epithelium and there is focal inflammation in the interstitial tissues. These changes have been explained in several ways; blockage of the tubules by casts cannot alone account for suppression of urine because only a few of the available tubules are, in fact, blocked. Young (1942) has shown that anuria is not related to shock and the reduction of renal arterial blood pressure. Tubular injury, sufficient in extent to prevent them from functioning, would lead to the passage of enormous quantities of glomerular filtrate if the glomeruli were working normally at the same time. This suggests that anuria in these cases is due to the cessation of formation of glomerular filtrate. A deviation of renal blood supply from the cortex to the medulla, as shown to take place in animals under experimental conditions by Trueta and his co-workers (1947), explains the appearance of the kidney in these cases with its ischemic cortex and engorged medulla, and also supplies a reason for glomerular failure. Early on in the disease the shunt allows a small amount of filtration through the juxtamedullary glomeruli, and this filtrate is excessively concentrated in the tubules, which are normally those in which water reabsorption takes place to the greatest extent. Casts are thereby formed in these tubules and any toxin present in the glomerular filtrate is also concentrated within their lumina. In the initial stages, therefore, a concentrated urine with casts is secreted, but later on the tubules, damaged from local toxin action, are no longer able, selectively, to reabsorb water from the glomerular filtrate, and they pass it on as a very dilute urine.

What then is the possible connexion, if any, between these two different pathological conditions? All the available evidence points to there being a circulating toxin involved, always in cortical necrosis, often in lower nephron nephrosis. It is conceivable that, following a sudden release of toxic products into the circulation as, for example, following the absorption of uterine muscle breakdown substances in concealed accidental hemorrhage, the kidney deals with the toxin presented to it in one of two ways: Either a protective mechanism is brought into effect, and, by means of a remote neurovascular or local toxin-induced mechanism, the blood with its toxin is deviated from the cortex to the medulla so as to save the cortex from the action of this toxin; or else this protective mechanism fails and the specially susceptible cortical vessels become injured by the toxin, paralysed, engorged, and, finally, blocked. In the first case we get lower nephron nephrosis and in the second cortical necrosis.

(3) *Recovered cases of anuria*.—The only essential difference between these and the fatal cases as regards clinical history seems to be that in cases which recover urinary secretion starts and improvement begins. It is interesting to note that in spite of diuresis the blood urea increases in amount for a few days after the period of the anuria but with the gradual recovery of the renal tubules more and more water is reabsorbed, the urinary urea concentration rises and the blood-urea level falls to normal. Time is a vital factor determining recovery from anuria. As Gibberd said in 1936: "So long as the patient does not die from uræmia, or from some other complication in the meantime, time alone will result in more and more recovery." Unfortunately, it is impossible to distinguish with certainty on clinical grounds between cortical necrosis and lower nephron nephrosis. A consideration of the pathology in each condition is enough to demonstrate that cortical necrosis in all stages is inevitably fatal, while, on the other hand, there is no reason to suppose that most cases of lower nephron nephrosis will not recover, given time. Conversely, the cases which recover have been suffering from lower nephron nephrosis, not cortical necrosis. In support of this a functional ischaemia of the renal cortex produced by experimental means has never, so far as I am aware, caused necrosis and therefore necrosis should not be regarded as being

There is ample anatomical and experimental evidence which indicates the functional specialization of the peripheral intralobular arteries and afferent arterioles, and it may well be that this functional individuality renders these vessels more susceptible to damage by agents responsible for vasomotor sensitivity, and that is an inherent factor in the pathology of cortical necrosis of the kidney in pregnancy.

## REFERENCES

- DE NAVASQUEZ, S. (1935) *J. Path. Bact.*, **41**, 385.  
 — (1938) *J. Path. Bact.*, **46**, 47.

Mr. T. L. T. Lewis: The clinical picture presented by cases of anuria in obstetrics should be kept in mind when attempts are made to explain the pathological mechanisms involved. All cases, with the exception of some of those occurring as the result of sulphonamide therapy, can be grouped as follows:

- (1) Fatal cases of anuria in which a diagnosis of symmetrical cortical necrosis of the kidneys is made post mortem.
- (2) Fatal cases of anuria in which a diagnosis of lower nephron nephrosis is made post mortem.

- (3) Recovered cases of anuria, in a few of which a kidney biopsy has been made.

The first and second of these groups contain the fatal cases in which an essential difference can be made on a basis of morbid anatomy, but they are fundamentally different, also, in the way in which their final pathological features are produced. Certain precipitating factors seem to be common to both, however, such as concealed accidental hæmorrhage, eclampsia and traumatic delivery; although a greater variety of factors predisposes to lower nephron nephrosis as, for instance, blood transfusion reaction, septic abortion and crush injury, conditions which have hitherto not been reported as being followed by cortical necrosis. Perhaps the most striking feature of these two pathological extremes is the similarity of their clinical pictures. I propose to consider the two conditions, cortical necrosis and lower nephron nephrosis in obstetrics, separately, in order to bring out this clinical similarity and pathological difference.

(1) *Cortical necrosis*.—This condition comes on chiefly following concealed accidental hæmorrhage or eclampsia and rarely after traumatic delivery. In 1941 Duff and More of Montreal analysed 71 reported cases of cortical necrosis of which 48 had occurred in pregnancy. Of these 48 cases two-thirds were in patients over the age of 30, 50% had been preceded by accidental hæmorrhage and 25% by eclampsia. Nearly all of them had a premature labour, but 16 had neither an accidental hæmorrhage nor a toxæmia, and 14 followed delivery before the 28th week. At the start of the disease the withdrawal by catheter of a few ounces of heavily blood-stained urine from the bladder heralds the onset of anuria. This warning hæmaturia is replaced by the daily secretion of a very small quantity (an ounce or two) of a very dilute urine resembling almost glomerular filtrate; such an anuric state persists until death takes place about the tenth to the twelfth day, as a rule. In spite of almost complete anuria, with steadily rising blood-urea and blood-potassium levels, the patient remains remarkably alert and cheerful and free from symptoms until very near the end, when she subsides into a coma and dies. Not uncommonly this classical appearance is altered by a complication such as persisting vomiting or diarrhoea, by low plasma proteins and œdema, or by severe anæmia or even by the result of energetic measures which are undertaken to stimulate renal secretion.

Turning now to the pathological features, we are familiar with the complete necrosis of the greater part of the kidney cortex, the so-called thrombi filling the glomerular afferent arterioles and capillaries, and the interlobular arteries, and the remarkable freedom of the medullary tubules from pathological change.

De Navasquez has contributed largely to our knowledge of the pathogenesis, by his experiments on rabbits with staphylococcal toxin, demonstrated at this Discussion, whereby he was able to show that even in the earliest stages of development of necrosis the renal cortex is tremendously engorged with blood, and the eventual ischaemic necrosis is brought about by a failure of blood to circulate through a cortex stuffed with red blood cells: he and other workers have shown that an underlying vascular injury (in fact an arterial wall necrosis) is responsible for the circulatory occlusion and when this has happened the condition is irreversible. Now, without blockage of the afferent glomerular vessels, there is no reason to suppose that filtration ceases so that the onset of anuria in this condition denotes the permanent cessation of glomerular filtration. Initially marked vascular engorgement of damaged glomerular capillaries permits some red cells to escape into the urine, but, soon after, glomerular filtrate only, from functioning glomeruli in the corticomedullary zone, passes into the bladder through renal tubules which have lost their power of water reabsorption. Such a loss of function on the part of the tubules is not surprising, for large segments of almost every nephron are involved in the affected part of the cortex.

fell on the day of delivery and then rose for the succeeding ten days. The blood urea on the eighth day was 42 mg. %.

**CASE II.**—Mrs. T., aged 20, primigravida. Normal until 34th week of pregnancy, when the blood-pressure was slightly raised (138/60) above the previous level. Two weeks later the blood-pressure was 140/72 and there was some albuminuria and edema of the legs. One week later the blood-pressure was again 140/77, edema was more marked and there was a trace of albumin in the urine. She was admitted to hospital that day. She complained of some headache that evening; her blood-pressure was 164/96 but fell to 140/84. The following morning blood-pressure was 154/94. The patient felt well and had no complaints. Blood urea was 75 mg. %; urea clearance was 16%; urinary output in twenty-four hours was 50 oz. The following morning she complained of a headache at 5 a.m. and had four eclamptic convulsions in quick succession. She was comatose and never regained consciousness. Blood-pressure ranged between 180/90 and 170/100. Death occurred forty-four hours later. Blood urea on the day before death was 207 mg. %; urine urea was 190 mg. %. Urinary output in the forty-four hours preceding death was 17 oz. Post-mortem showed extensive subarachnoid hemorrhage over left cerebrium and cerebellum and occasional accidental hemorrhages in the uterus. Microscopic examination of liver showed some hemorrhages amongst the liver cells. Kidney showed typical eclamptic changes; the glomeruli had thickening of the basement membrane of the capillaries and were relatively avascular and the tubules were normal.

Subarachnoid hemorrhage is a cause of pre-renal uræmia but it could not account for the marked rise of blood urea which occurred in this case. The glomerular changes in the kidney were marked and there was very little blood present. The ischemia in the glomeruli may in this case, at least, have been the cause of the renal failure and possibly also of the hypertension.

**Mr. John Sophian:** Despite the observation that the glomeruli are found to contain a great deal of blood in certain cases of oliguria, regard the primary change in them to be of an ischemic nature. Here I would invoke the observation of Dible and Moore on the usual histological findings and would explain the fullness of the glomeruli as the result of an eventual paralysis overtaking the vessel wall as Oertel suggests.

Clinically lower nephron nephrosis and bilateral cortical necrosis are found as complications of concealed accidental hemorrhage. Occasionally they are preceded by eclampsia without accidental hemorrhage intervening. Concealed accidental hemorrhage may arise in a previously healthy pregnant woman, and may give rise to pre-eclamptic toxæmia in her. It seems therefore that certain changes occur in the kidney which are provoked by these presumably allied causes. In my opinion cortical ischemia of varying degree explains these "toxæmic" manifestations of pregnancy. Pre-eclamptic toxæmia is at one end of the scale with bilateral cortical necrosis at the other. The mechanism of the Oxford shunt is primarily one of cortical ischemia. Associated with it is the by-pass pathway. It is therefore probable that it is operative in these manifestations.

In lower nephron nephrosis the proximal portions of the nephron tend to survive, whereas the distal succumb. Deprivation of the blood supply would be more acutely felt at the latter level because of the greater physiological functioning and consequent greater oxygen needs. Some glomerular filtration could explain the presence of the "hæm" products in the tubal lumen though I believe these have an intrarenal origin almost entirely.

Odell and Lampert have inferred that the glomerular circulation is cut down in pregnancy toxæmia from the experimental evidence they have adduced. The latter has shown that the afferents of the glomerulus are in spasm. Dr. G. M. Bull has also indicated that the renal blood flow is reduced in the early stages of anuria. These findings would fit in with the theory of cortical ischemia. The compensatory effects of a by-pass on the blood flow may become insufficient as the spasm increases.

Invoking cortical ischemia as the basis of these manifestations I wish to submit that resistance to stretching of the uterine muscle is the factor responsible for initiating the renal change. The stimulus may be of a nociceptive order, or may arise from alterations in the vascular supply of the resisting uterine wall.

Clinically resistance to stretch is occurring in the primiparous rather than the multiparous uterus, in late pregnancy rather than early, in twins, in hydramnios, in hydatidiform mole and in concealed accidental hemorrhage, conditions frequently associated with the toxæmic syndrome. That all primiparæ do not suffer from it may have to do with the variable faculty of individual uterine muscle to resist stretch (Schumacher) and to the maintenance of the pear shape of the uterus beyond the second trimester (Reynolds). Post-partum eclampsia is probably due to the failure of the relief of renal spasm present during pregnancy. This may be prolonged by the continuing needs of the puerperal uterus for large amounts of blood that renal cortical ischemia may help to provide and by the lessened post-partum blood-pressure being unable to overcome it.

The theory of spasm will be more acceptable when we appreciate that complete recovery from the toxæmic state is almost invariable, and that it does not tend to repeat itself in subsequent pregnancies.

due merely to an exaggeration in degree of the same mechanism, namely, vascular spasm, which results always in lower nephron nephrosis. If it were so, one would expect in cortical necrosis to find evidence of the tubular lesions usually found in lower nephron nephrosis, but, in fact, these lesions are conspicuously absent.

Reference to the cases reported as recovering from cortical necrosis shows that most have been diagnosed on clinical grounds only, which is not enough to differentiate them from lower nephron nephrosis. Of the cases in which a biopsy has been obtained at the same time as decapsulation was performed, that reported by Crook in 1926 is worth further consideration. In his case, accepted as a case of cortical necrosis, the lesion is a focal one and a large part of the specimen removed shows healthy cortex. But the lesions present cannot account for the presence of anuria unless we suppose that the healthy tissues were excluded from the circulation by a corticomedullary shunt and that, although there is undoubted evidence of focal cortical necrosis, we are dealing with a case of lower nephron nephrosis as far as the anuria is concerned.

In conclusion, may I draw your attention to the phases through which consideration of the pathological features of cortical necrosis has passed. At first, the condition was recognized only at post-mortem and cases which recovered were labelled "Suppression of urine of unknown aetiology". And then it was pointed out how similar was the clinical sequence of events in both groups of cases and they were regarded as the same in pathology; that is, both cortical necrosis. Finally, we recognized two pathologies, cortical necrosis which is always fatal, and lower nephron nephrosis which, although occasionally demonstrable post mortem, accounts for all the cases which recover. Thus, we seem to be dealing with varying degrees of kidney damage due to the same factor, probably toxic in nature. In most cases there is relatively little toxin which is harmlessly shunted through the kidney medulla for so short a time that urinary secretion is hardly diminished. Next in severity are those, referred to as lower nephron nephrosis, in which a larger amount of toxin is shunted through the medulla so as to spare the cortex but to produce tubular necrosis. And, lastly, there are the cases of cortical necrosis in which an overwhelming dosage of toxin reaches and injures the cortical vasculature, through failure of the protective corticomedullary shunt to come into operation.

#### REFERENCES

- CROOK, A. (1927) *Proc. R. Soc. Med.*, 20, 1249.  
 DE NAVASQUEZ, S. (1935) *J. Path. Bact.*, 41, 385.  
 DUFF, G. L., and MORE, R. H. (1941) *Amer. J. med. Sci.*, 201, 428.  
 GIBBERD, G. F. (1936) *J. Obstet. Gynec.*, 43, 60.  
 TRUETA, J., BARCLAY, A. E., DANIEL, P. M., FRANKLIN, K. J., and PRICHARD, M. M. L. (1947) *Studies of the Renal Circulation*, Oxford.  
 YOUNG, J. (1942) *Brit. med. J.* (ii), 715.

**Miss Gladys Dodds:** Persistence of hypertension after delivery was observed in seven fatal cases of bilateral cortical necrosis of the kidney. All cases were associated with accidental hæmorrhage and raised blood-pressure. One patient had chronic hypertension, three had pre-eclamptic toxæmia and in the remaining three cases the ante-natal care was inadequate, so that the differential diagnosis between chronic hypertension and pre-eclamptic toxæmia could not be made. Six of the seven patients lived seven to ten days after delivery and onset of the anuria, and one lived twenty-eight days.

Two additional cases of accidental hæmorrhage, in whom the blood-pressure was normal during the pregnancy, had transient anuria lasting twenty-four to forty-eight hours after delivery. In both these cases the blood-pressure rose and remained raised for ten days. The probable diagnosis in these cases is a minor degree of renal cortical necrosis. It is reasonable to assume that the renal failure in these two cases is due to a temporary ischæmia of the kidneys and to associate the hypertension which occurred in them, as well as in those cases which terminated fatally, with the renal ischæmia.

In the majority of cases of pre-eclamptic toxæmia there is a dramatic fall in the height of the blood-pressure immediately after delivery, but in a small number of cases the raised blood-pressure may persist for some days. Four eclamptic patients were observed in whom, in addition to the raised blood-pressure, there was oliguria and renal failure. Details of two of these cases are given.

**CASE I.**—Mrs. B., primigravida, aged 28, had four eclamptic convulsions. On admission the blood urea was 26 mg.%, intake of fluid in the first twenty-four hours was 50 oz., output was 4 oz. urine and 10 oz. vomit. In the second twenty-four hours intake was 38 oz., output 9 oz. On the third day the patient was delivered and the intake and output were not estimated. In the first twenty-four hours after delivery the output was 14 oz., although the intake was 80 oz. Thereafter in the succeeding two twenty-four-hour periods, the output was 40 oz. and 60 oz. (Average output of urine after normal pregnancy and labour is 80–100 oz. daily in the first two days after delivery.) The blood-pressure

prolapse. (2) The Mayo operation (1915) in which, after vaginal hysterectomy has been performed, the broad ligament pedicles are joined together and interposed beneath the bladder, and the shortened cardinal ligaments are also united in the mid-line. The chief defect in this operation is the not infrequent occurrence of an enterocele. Everard Williams (1937) has described a modification of the Mayo operation for procidentia, in which a posterior colporrhaphy approach gives maximal exposure of the pouch of Douglas, and includes suture of the utero-sacral ligaments to prevent the subsequent development of an enterocele. Interposition of the sutured broad ligaments beneath the bladder is unnecessary if the pubo-cervical fascia is repaired. From some experience of this operation, which gives good results, but it must be admitted that the dissection is long and sometimes difficult, a considerable disadvantage in an obviously feeble patient. For this reason I believe that an abdominal approach should be considered in cases of procidentia.

Fixation of the cervix or vaginal vault to the round ligaments or ovarian pedicles is often practised in the course of an abdominal hysterectomy, but it is inadequate when vault prolapse is present, and in such cases the vault to the abdominal wall has occasionally been carried out. Brady (1936) proposed the use of the vaginal vault to the abdominal wall with braided silk sutures, and Grant (1938) has used preserved strips of fascia lata. A sling of external oblique aponeurosis has been used most successfully to suspend the bladder neck and urethra, in the Millin-Read operation for stress incontinence, and this has suggested the following technique for vault suspension.

#### TECHNIQUE OF OPERATION

A slightly curved transverse incision is made in the lower abdomen, with the patient in the Trendelenburg position, and two fascial strips of aponeurosis are prepared and left attached to muscle at each end. The rectum is then separated and the peritoneal cavity is opened. Subtotal or total hysterectomy is performed, and this is usually a simple procedure when the uterus is atrophic and the broad ligaments allow it to be brought well up into the wound. The fascial strips are now passed retroperitoneally with a round ligament forceps into the pelvis, where they are sutured with a fascia needle to the cervix or vaginal vault. The free end of each fascial strip is then withdrawn by the round ligament forceps and sutured to its point of origin. This forms a double sling supporting the cervix or vaginal vault at or slightly above its normal position in the pelvis. There is no fixation to the median part of the anterior abdominal wall to interfere with bladder function. The operation should be completed by obliteration of the elongated pouch of Douglas, to prevent the development of an enterocele. This may be accomplished by simple peritoneal approximation of the utero-sacral ligaments, or by obliterating purse-string sutures, as described by Moschowitz (1912). The pelvic peritoneum is then sutured and the abdomen closed.

This operation, which I have called vault-suspension, has been performed on four occasions, and the results in 3 cases after six months are entirely satisfactory. The fourth has not yet been followed up (see Table I). It must be repeated that the operation is intended only for cases of procidentia, and not for lesser degrees of vault prolapse, for which the

TABLE I.—VAULT SUSPENSION OPERATION

|       | Age | Parity | Condition                                                    | Date of operation |
|-------|-----|--------|--------------------------------------------------------------|-------------------|
| A. W. | 64  | C7 M3  | Procidentia 14 years. Stress incontinence 1 year             | 11.3.48           |
| A. B. | 73  | C4 M?  | Procidentia 6 months with ulceration of cervix and rectocele | 13.4.48           |
| M. B. | 51  | C3 M1  | Procidentia 6 months                                         | 24.4.48           |
| A. G. | 78  | C5 M?  | Procidentia 6 years with ulceration of cervix                | 18.1.49           |

Manchester operation remains the operation of choice. It might, however, be considered when an abdominal hysterectomy is required for some lesion of the uterus co-existing with vault prolapse. When marked cystocele or rectocele is present as well as procidentia, a vaginal approach is perhaps necessary, but I have been surprised at the disappearance of true cystocele and rectocele, with complete relief of symptoms, after the operation of vault-suspension.

The advantages claimed for this technique are that it is less traumatic and less likely to be followed by sepsis and urinary complications than the Mayo (1915) operation or its modifications. Further, the use of fascial strips to suspend the cervix or vaginal vault is considered to be more likely to produce a satisfactory and permanent result than the use of the normal supporting ligaments when these have become atrophic. Further experience will show whether



[February 18, 1949]

**Vault-Suspension**

By HUMPHREY G. E. ARTHURE, M.D., F.R.C.S., M.R.C.O.G.

THIS short paper describes a new surgical procedure for the treatment of vault prolapse. The latter may be described as a hernia of one or more pelvic viscera through the vaginal aperture in the pelvic diaphragm.

For many years it has been taught that the pelvic diaphragm, formed by the levator ani muscles, actively supports the pelvic viscera, a misconception which has greatly influenced the surgical treatment of genital prolapse. It is well known that prolapse may never occur in a patient with a complete perineal tear, which markedly widens the aperture between the levators; and that it may occasionally occur in a nulliparous patient with a normal pelvic diaphragm. In point of fact the bladder and cervix are normally situated some distance above the levators, and, as far as I know, there is no reflex contraction of these muscles when the intra-abdominal pressure is raised. It must therefore be clearly recognized that suture of the levator muscles should not be an essential part of an operation for cystocele or vault prolapse, and that narrowing of the vaginal introitus by suturing the inner free borders of these muscles must be carefully avoided when the perineum is being repaired.

Cystocele and rectocele are the result of weakness of the pubo-cervical fascia and fascia propria of the rectum respectively. I am not impressed with the widely held view that these forms of genital prolapse cause descent of the uterus by pulling on the cervix, and maintain that vault prolapse is essentially due to stretching of the lateral cervical or cardinal ligaments and the utero-sacral ligaments. In vault prolapse the bladder inevitably descends with the cervix, even though the pubo-cervical fascia may be intact, and the term pseudo-cystocele has been used to distinguish it from a true cystocele, due to weakness of the pubo-cervical fascia. Again, the peritoneum of the pouch of Douglas is closely connected with the cervix and posterior fornix of the vagina, and the pouch inevitably elongates in vault prolapse, to form a potential or actual enterocele. It is interesting to note here that elongation of the pouch of Douglas is considered by Moschowitz (1912) to be the first stage in the formation of a rectal prolapse. Rectocele does not inevitably or usually accompany vault prolapse, because the fascia propria of the rectum is attached to the utero-sacral ligaments and not to the cervix.

I do not intend to discuss the ætiology of genital prolapse at length, and it is accepted that the commonest factor is over-stretching of the pelvic fascial structures during parturition. Involution of these structures will often lessen the degree of prolapse, whatever post-natal treatment is adopted. Consequently the more marked cases of prolapse usually present for treatment at the end of the child-bearing period or after the menopause, when atrophic changes due to age and oestrogen deficiency make the fascial structures less able to withstand any increased intra-abdominal pressure.

**TREATMENT**

In the surgical treatment of uterine prolapse it is obvious that hysterectomy alone, with or without removal of the cervix, cannot cure the prolapse, and in this communication the term vault prolapse is used so as to include those cases in which the uterus has already been removed. Attempts to cure vault prolapse by narrowing the vaginal introitus are basically unsound. Early gynaecological surgeons found no difficulty in curing cystocele and rectocele by vaginal plastic operations, but they relied on fixation of the uterus to the abdominal wall in cases of vault prolapse. This operation has now fallen into disrepute, chiefly because the fixation was impermanent, prolapse recurring with the uterus still attached by a long band to the abdominal wall; occasionally, with the fixation satisfactory, an enterocele would develop behind the cervix.

The first great advance in the surgical treatment of vault prolapse was the Manchester operation, of which the history has been described by Sir Wm. Fletcher Shaw (1933). In this operation the lateral cervical or cardinal ligaments are approximated in front of the cervix, after partial amputation; this tends to shorten the ligaments and displaces the cervix upwards and backwards. It is entirely satisfactory in first and second degrees of vault prolapse, but in procidentia the cervical stump remains at the vaginal introitus after the key sutures through the cardinal ligaments have been tied, and therefore a well-done perineorrhaphy is advocated to conceal the residual laxity of the vaginal vault.

Two alternative procedures have also been practised: (1) Interposition of the uterine body beneath the bladder was recommended by Watkins (1899) for the treatment of cystocele and uterine prolapse after the menopause. This operation does not include repair of the uterine supports, and reliance is again placed on a perineorrhaphy to support the vault

prolapse. (2) The Mayo operation (1915) in which, after vaginal hysterectomy has been performed, the broad ligament pedicles are joined together and interposed beneath the bladder, and the shortened cardinal ligaments are also united in the mid-line. The chief defect in this operation is the not infrequent recurrence of an enterocele. Everard Williams (1937) has described a modification of the Mayo operation for procidentia, in which a posterior colporrhaphy approach gives a good exposure of the pouch of Douglas, and includes suture of the utero-sacral ligaments to prevent the subsequent development of an enterocele. Interposition of the utero-sacral ligaments beneath the bladder is unnecessary if the pubo-cervical fascia is repaired. In some experience of this operation, which gives good results, but it must be admitted that the dissection is long and sometimes difficult, a considerable disadvantage in an elderly and feeble patient. For this reason I believe that an abdominal approach should be considered in cases of procidentia.

Fixation of the cervix or vaginal vault to the round ligaments or ovarian pedicles is often practised in the course of an abdominal hysterectomy, but it is inadequate when vault prolapse is present, and in such cases the abdominal wall has occasionally been carried out. Brady (1936) proposed suspending the vaginal vault to the abdominal wall with braided silk sutures, and Grant (1938) has used preserved strips of fascia lata. A sling of external oblique aponeurosis has been used most successfully to suspend the bladder neck and urethra, in the Millin-Read operation for stress incontinence, and this has suggested the following technique for vault suspension.

#### TECHNIQUE OF VAULT SUSPENSION OPERATION

A slightly curved transverse incision is made in the lower abdomen, with the patient in the Trendelenburg position, and two strips of aponeurosis are prepared and left attached to muscle at each end. The incision is then separated and the peritoneal cavity is opened. Subtotal or total hysterectomy is performed, and this is usually a simple procedure when the uterus is atrophic and the ligaments allow it to be brought well up into the wound. The fascial strips are then fixed retroperitoneally with a round ligament forceps into the pelvis, where they are secured with a fascia needle to the cervix or vaginal vault. The free end of each fascial strip is then withdrawn by the round ligament forceps and sutured to its point of origin. This forms a double sling supporting the cervix or vaginal vault at or slightly above its normal position in the pelvis. There is no fixation to the median part of the anterior abdominal wall to interfere with bladder function. The operation should be completed by obliteration of the elongated pouch of Douglas, to prevent the development of an enterocele. This may be accomplished by simple peritoneal approximation of the utero-sacral ligaments, or by obliterating purse-string sutures, as described by Moschowitz (1912). The pelvic peritoneum is then sutured and the abdomen closed.

This operation, which I have called vault-suspension, has been performed on four occasions, and the results in 3 cases after six months are entirely satisfactory. The fourth has not yet been followed up (see Table I). It must be repeated that the operation is intended only for cases of procidentia, and not for lesser degrees of vault prolapse, for which the

TABLE I.—VAULT SUSPENSION OPERATION

|       | Age | Parity | Condition                                                    | Date of operation |
|-------|-----|--------|--------------------------------------------------------------|-------------------|
| A. W. | 64  | C7 M3  | Procidentia 14 years. Stress incontinence 1 year             | 11.3.48           |
| A. B. | 73  | C4 M2  | Procidentia 6 months with ulceration of cervix and rectocele | 13.4.48           |
| M. B. | 51  | C3 M1  | Procidentia 6 months                                         | 24.4.48           |
| A. G. | 78  | C5 M2  | Procidentia 6 years with ulceration of cervix                | 18.1.49           |

Manchester operation remains the operation of choice. It might, however, be considered when an abdominal hysterectomy is required for some lesion of the uterus co-existing with vault prolapse. When marked cystocele or rectocele is present as well as procidentia, a vaginal approach is perhaps necessary, but I have been surprised at the disappearance of true cystocele and rectocele, with complete relief of symptoms, after the operation of vault-suspension.

The advantages claimed for this technique are that it is less traumatic and less likely to be followed by sepsis and urinary complications than the Mayo (1915) operation or its modifications. Further, the use of fascial strips to suspend the cervix or vaginal vault is considered to be more likely to produce a satisfactory and permanent result than the use of the normal supporting ligaments when these have become atrophic. Further experience will show whether

this operation of vault-suspension is indeed a satisfactory and worthy operation for procidentia.

## REFERENCES

- BRADY, L. (1936) *Amer. J. Obstet. Gynec.*, 32, 295.  
 GRANT-WARD, E. (1938) *Arch. Surg.*, 36, 163.  
 MAYO, C. H. (1915) *Surg. Gynec. Obstet.*, 20, 235.  
 MILLIN, T., and READ, C. D. (1948) *Postgrad. med. J.*, 24, 268, 51.  
 MOSCHOWITZ, A. V. (1912) *Surg. Gynec. Obstet.*, 15, 7.  
 SHAW, W. F. (1933) *Amer. J. Obstet. Gynec.*, 26, 667.  
 WATKINS, T. J. (1899) *Amer. J. Obstet. Gynec.*, 15, 420.  
 WILLIAMS, H. G. E. (1937) *Proc. R. Soc. Med.*, 30, 1282.

Mr. Charles Read said that Mr. Arthure's application of the sling for the cure of uterine descent might with advantage be applicable to certain cases of prolapse without cystocele and rectocele—in vaginal vault prolapse. Mr. Read had not used this procedure but it might prove useful in certain cases. He disagreed with Mr. Arthure's statement that procidentia could not be cured by the Manchester operation. Nearly all such cases could be treated with success by that operation except perhaps in those in which there was complete vaginal evagination. In a previous discussion on the subject, the impression obtained by reading the *Proceedings* (1948, 41, 676) was that nothing but vaginal hysterectomy and repair offered any chance of success. He would like to record his disagreement with such a sweeping impression.

Mr. Douglas MacLeod thought that Mr. Arthure's ingenious operation might prove invaluable in treating cases of procidentia occurring in elderly nulliparous women and in those cases of vaginal prolapse occurring in women in whom the uterus had been removed. He could not agree that a well-performed Manchester operation was not able to cure a complete procidentia.

Mr. Arthure, in reply to Mr. Read, said he did not consider the Manchester operation was entirely satisfactory for procidentia, even though some surgeons claimed satisfactory results. One of his cases had had a large ulcer of the cervix, which was eliminated by total hysterectomy and the fascial strips were then passed through the sutured vaginal vault.

## Some Aspects of Non-Gonococcal Infections of the Genital Tract. [Abridged]

By A. H. HARKNESS, M.R.C.S., L.R.C.P.

NON-GONOCOCCAL discharges in women, as in men, have a very varied ætiology. I have been asked to consider only those which are presumed to be due either to a virus or pleuropneumonia-like organisms. First I shall consider the cases due to a virus.

In the study of the virus disease known as *inclusion cervicitis* it is necessary at the same time to take into consideration *inclusion urethritis* in the male and *inclusion conjunctivitis* in babies. The infective agent is believed to be the same in all three diseases. This is shown not only by the large number of cases reported in the literature in which the infections have been passed from one person to another, but also by human and animal inoculation experiments. The male and female are infected during sexual intercourse (especially during and immediately before or after a period), and the baby from the passage of the head through the infected genital tract of the mother. It must also be mentioned, however, that inclusion blennorrhœa ("swimming-bath conjunctivitis") in adults and sometimes urethritis and cervicitis may be contracted in swimming baths containing the virus. This has reached the water either from the genital tract of the female or, more probably, from urination whilst bathing.

Two accidental infections have been reported in the literature, one by Thygeson and Mengert (1936), and the other by Julianelle (1937). In the former a gynaecologist's eye was infected by a spurt of blood during an operation for dilatation of the cervix with curettage; in the latter a jet of infected fluid splashed into a nurse's eye during treatment of a case of inclusion blennorrhœa. It is interesting to note that in both cases immediate prophylactic treatment failed to prevent infection. It has already been shown by several workers that women suffering from inclusion cervicitis may infect their own eyes. Infection in such cases may be conveyed to the eyes either by contaminated fingers or by the blood-stream.

The inclusion bodies of inclusion cervicitis, morphologically indistinguishable from those of trachoma and the lymphogranuloma-psittacosis-pneumonitis group, consist of discrete granules lying free or in the cytoplasm of epithelial cells. Other larger bodies, first described

by Lindner (1910) and known as initial bodies, are seen in early inclusions, sometimes extracellular in position. They take on a violet or red stain with Giemsa. No worker has yet succeeded, however, in culturing the virus.

[For reference to the literature on this subject, see Bibliography, p. 392.]

Most of my own work has been carried out on the contacts of men suffering from subacute (Waelisch) and acute abacterial urethritis—types of non-gonococcal urethritis in which intracytoplasmic inclusion bodies and free elementary bodies are frequently demonstrated in urethral scrapings.

*Pleuropneumonia-like or "L" organisms.*—The organism of pleuropneumonia, until recently regarded as a virus, is now considered to occupy a place intermediate between bacteria and viruses. Unlike viruses these organisms are able to grow on a number of non-living media, but they resemble viruses, however, in being filtrable through bacteria-proof filters during the granular phase of their development.

The first member of this group of organisms was isolated by Nocard and Roux in 1898 from contagious pleuropneumonia of cattle. A similar organism was found by Bridré and Donatien (1923, 1925), in sheep and goats suffering from agalactia. Other strains of organisms of the same group, usually referred to as pleuropneumonia-like or "L" organisms, have been described as causing arthritis and other conditions, chiefly in rats and mice.

In recent years organisms of the group have been identified in the urogenital tracts of both men and women. (A complete review of the literature on pleuropneumonia is given by Harkness and Henderson-Begg (1948).)

In some of my cases in which cultures were positive for "L" organisms, Giemsa-stained smears showed the cytoplasm of the epithelial cells to be packed with bluish-stained bodies showing marked pleomorphism; spherules, ovoids, rickettsia-like forms and elementary bodies being observed with a high proportion of ring-like forms: these bodies were also seen lying free. The presence of "L" organisms in the secretions can, in my opinion, often be determined by the examination of smears alone and in a large majority of such cases cultural confirmation can also be obtained.

I know of no distinctive clinical characteristics of vaginal discharges from which scrapings show the presence of inclusion bodies presumed to be due to a virus, and this also applies to those in which "L" organisms are found in the secretions. It should be remembered, however, that both conditions, as already mentioned, may be associated in mixed infections with other diseases. In some cases the discharge is profuse and in others scanty. I have on many occasions cultured "L" organisms from the female contacts of men suffering from non-gonococcal urethritis in which the signs of cervical or vaginal infection were slight. One such case infected three men over a period of twelve months, two with uncomplicated abacterial urethritis and one in which the infective agent became blood-borne to cause bilateral conjunctivitis, polyarthritis and keratoderma blennorrhagica—the complete Reiter syndrome.

I have on several occasions cultured "L" organisms in both men and women in investigations for sterility, and in this respect it is interesting to note that Edward and his collaborators (1947) isolated these organisms from 18 of 64 cows from herds with long-standing histories of infertility ascribable to no known cause; similar organisms were isolated from the semen of 6 bulls.

*The significance of inclusions and the isolation of "L" organisms from cervix and vagina.*—Inclusion bodies are more easily demonstrated in scrapings from conjunctiva and cervix than from the urethra. This, in all probability, is due to the difficulty (owing to pain) in taking adequate scrapings from so sensitive a structure as the urethral mucosa. In the treatment of cases presumed to have a virus aetiology it is difficult to understand why inclusion blennorrhœa reacts so favourably to sulphonamide therapy, whereas inclusion cervicitis and urethritis (due to a virus or "L" organisms) are, in my experience, commonly resistant to these drugs. Streptomycin may prove to be the drug of choice in the treatment of these conditions as both animal and human strains of "L" organisms are susceptible to low concentrations of this antibiotic. I know of no work that has been carried out in an attempt to incriminate "L" organisms in inclusion blennorrhœa.

In some of my cases (those in which "L" organisms are cultured and only elementary bodies are seen) I have found it extremely difficult to decide whether the granules signify disease due to a virus or whether they represent the granular phase in the development of "L" organisms (Harkness, 1945).

There are also workers who suggest that "L" organisms may be saprophytes in the female and that only under certain conditions do they cause urethritis in the male. Klieneberger-Nobel (1945) stated that her investigations showed that it was very rare to find "L" organisms in the vagina of normal women. They were detected in only 7 of 50 pregnant women attending an ante-natal clinic and of these 5 had suffered or were still suffering from inflammatory complications of pregnancy. Salaman isolated "L" organisms

in 6% of normal women and Beveridge and his collaborators in 17 of 101 apparently normal women attending a gynaecological clinic—perhaps not the place to select so large a number of normals. In my small series cultures were negative in all. Urethral washings from 50 normal men were also negative, an observation agreeing with that of Beveridge and his collaborators who carried out cultural investigations on 67 medical students with completely negative results. On the other hand, Salaman reported "L" organisms in 4 of 28 men from a skin department but admitted that one with positive findings showed a slight pyuria. Of course it is possible that there is more than one species of "L" organisms—one being commensal and the other pathogenic—indeed Edward (in press) has shown that this is so in the bovine.

It was unfortunate that the very thorough investigation carried out by Bourne (1943) on many cervixes amputated for leucorrhœa did not take into consideration the possibility of a virus aetiology. He noted the comparative absence of true signs of inflammation and stressed an endocrine pathology.

Finally just a word about blood-borne complications from primary foci in the cervix. In the male I have seen more than a hundred cases of abacterial urethritis of venereal origin with one or more of the complications of conjunctivitis, arthritis, balanitis and keratoderma blennorrhagica (the syndrome may be complete or incomplete), whereas, in the female, Reiter's syndrome is extremely rare. I have only seen three cases in which inclusion cervicitis was associated with polyarthritis and keratoderma blennorrhagica. I have, however, had several others of polyarthritis in women in which "L" organisms have been isolated in the cervical secretions but in which the absence of skin lesions made diagnosis extremely difficult. It is interesting to note that in the female the dysenteric syndrome of Reiter's disease is more frequently associated with blood-borne complications. I believe the infective agent in both the venereal and dysenteric syndromes to be the same.

#### BIBLIOGRAPHY

- BEVERIDGE, W. I. B., CAMPBELL, A. D., and LIND, P. E. (1946) *Med. J. Aust.*, **1**, 179.  
 BOURNE, A. (1943) *Brit. J. vener. Dis.*, **19**, 3.  
 BRIDRÉ, J., and DONATIEN, A. (1923) *C.R. Acad. Sci., Paris*, **177**, 841.  
 ———, ——— (1925) *Ann. Inst. Pasteur*, **39**, 925.  
 DIENES, L., and EDSALL, G. (1937) *Proc. Soc. exp. Biol., N.Y.*, **36**, 740.  
 ——— (1940) *Proc. Soc. exp. Biol., N.Y.*, **44**, 468.  
 ———, and SMITH, W. E. (1942) *Proc. Soc. exp. Biol., N.Y.*, **50**, 99.  
 EDWARD, D. G. ff., HANCOCK, J. L., and HIGNETT, S. L. (1947) *Vet. Rec.*, **59**, 329.  
 ——— (1949) In the press.  
 FRITSCH, H., HOFFSTATTER, A., and LINDNER, K. (1910) *v. Graefes Arch. Ophthalm.*, **76**, 547.  
 HALBERSTAEDTER, C., and PROWAZEK, S. (1909) *Berl. klin. Wschr.*, **46**, 1839.  
 HAMILTON-PATERSON, J. L. (1948) *Brit. J. vener. Dis.*, **24**, 122.  
 HARKNESS, A. H. (1945) *Brit. J. vener. Dis.*, **21**, 93.  
 ———, and HENDERSON-BEGG, A. (1948) *Brit. J. vener. Dis.*, **24**, 50.  
 HEYMAN, B. (1910) *Berl. klin. Wschr.*, **47**, 663.  
 JULIANELLE, L. A. (1937) *Proc. Soc. exp. Biol., N.Y.*, **36**, 617.  
 KLIENEBERGER-NOBEL, E. (1945) *Lancet* (ii), 46.  
 NOCARD, E., and ROUX, E. (1898) *Ann. Inst. Pasteur*, **12**, 240.  
 SALAMAN, M. H. (1946) *J. Path. Bact.*, **58**, 31.  
 SORSBY, A. (1945) *Ophthalmia Neonatorum*, p. 29. London.  
 ———, HOFFA, E., and YOUNG, E. N. (1944) *Brit. J. Ophthalm.*, **28**, 451.  
 THYGESON, P. (1934) *Amer. J. Ophthalm.*, **17**, 1019.  
 ———, and MENGERT, W. F. (1936) *Arch. Ophthalm.*, **15**, 377.  
 ———, and STONE, W. (1942) *Arch. Ophthalm.*, **27**, 91.

## Section of Odontology

President—Professor SHELDON FRIEL, M.Dent.Sc., Sc.D., F.D.S.

[January 24, 1949]

### The Hypotheses Concerning the Ætiology of Dental Caries

By GILBERT J. PARFITT, M.R.C.S., L.R.C.P., F.D.S. R.C.S.

*Lecturer in Preventive Dentistry, Institute of Dental Surgery, Post Graduate Medical Federation*

#### *Collection and Assembly of Data*

Clinicians are in a position to make an enormous number of observations upon the event of dental caries. Caries is seen first in characteristic areas of the tooth surface, in pits and in fissures, at the gingival margin regardless of the stage of eruption of the tooth, and interproximally, immediately below the contact area upon whatever topographical surface of the tooth that may be. Interstitially and gingivally, caries appears upon the surface of the enamel either as a white opaque area, as a pigmented area without obvious loss of substance, or as roughening or pitting of the surface. Other plain surfaces of the tooth rarely become the site of commencement except under certain special circumstances. Some teeth are much more liable to caries than others and so are particular fissures upon the teeth.

The speed of the carious process varies considerably. The crown of a tooth of the temporary dentition may be completely disintegrated within six months of eruption, and serious damage to the enamel surface can occur within three weeks after the insertion of an appliance. On the other hand, a roughened and stained surface, or interstitial cavity detectable only by X-ray, may progress slowly for years. Some carious processes become arrested altogether particularly when an adjacent tooth is removed.

The enamel beneath greenish plaques commonly proves to be damaged, whereas there is one particular pigmented stain [1] in the form of a line parallel to the gingival margin which is associated with less than average caries. All members of some families are remarkably free from caries whilst other families show the reverse; some individual members of a family may be in marked contrast to the rest. An increase of caries incidence is noted during the 'teen age, and some individuals who have been free from caries for years suddenly present active caries. Clinical surveys of groups of individuals living under different conditions show variation in caries incidence [2]. Comparisons have been made of the caries incidence between different nations, between town and country folk, Institutional children and the Public School children of the same town [3], groups in parts of the same county and between neighbouring towns [4].

Many instances have been noted where the caries experience has altered. The remote peoples suffer an increase in caries when they come into contact with civilization [5]. Under wartime conditions the incidence decreases; this effect is shown to a different degree in each country, as has lately been experienced in Finland, Norway and England, only to increase again after the war period is over [6]. Many data have been gained by special observation and experiment in bacteriology, biochemistry and histology. Although the validity of some of the observations has been established beyond reasonable doubt, other observations require verification, and in some cases conclusions drawn from the valid observations are unjustified and untenable.

The difficulty workers have had in formulating hypotheses of the ætiology of dental caries which fit the facts suggests that a diversity of factors was involved, and that many of these are accidental, incidental or accessory to the cause, but nevertheless affect the speed of the carious process or its incidence. Only a few of the hypotheses which have been presented can be briefly surveyed here.

#### *Nutritional Factors*

If diet is accepted as having an effect upon the incidence of dental caries then the question arises whether this is brought about by nutrition or by local environment. The nutritional effect might be connected with the ingestion of any substance and may be due to its presence or absence in the diet. A nutritional effect might be produced by some change in the environment of the tooth surface such as an alteration of the saliva secretion, or the tooth structure may be affected during its formation.

It has been suggested that lymph gains access to the enamel surface by permeating the enamel cap [7] carrying with it a protective agent. Although enamel can act as a permeable and a semi-permeable membrane [8, 9] the degree would appear to be slight; and no measurements are known to have been made in the mouth, so the quantitative effect is unknown. Since root-filled teeth do not decay more readily than vital ones the effect cannot be of prime importance.

*Saliva.*—Caries commences on the surface of the tooth and as this surface is constantly

bathed by saliva, it would be reasonable to expect that alteration in the constituents of the saliva would have an effect upon caries.

A slight correlation between caries incidence and the variation in the composition and properties of the saliva has been shown. Broderick [10] considered the pH of the saliva was of prime importance but others find little correlation between caries and salivary pH. Hawkins [11] found a better correlation when the pH and the calcium and phosphorus content were taken together and was able to group by this means: Immune to decay, Immune with pyorrhœa, Active Decay and Erosion, and Class 5 cavities. He was satisfied that the cause of dental caries was a faulty acid-base and calcium-phosphorus balance and that he could alter this balance by dietetic means. Hawkins therefore ascribes preventive virtue to a diet moderate in protein, low in cereal, high in calcium and of high potential alkalinity. Other workers have had great difficulty in altering the pH of the saliva or its mineral content, and when any change was noted it was transient. The various peoples of the world, following their national food habits, are carrying out natural experiments on diet. Examination of these shows that the immunity and susceptibility to caries in the different areas is not explained by the hypothesis put forward by Hawkins, for some people living on a high cereal diet [12] show a considerable degree of immunity.

Clinically increase of tackiness of the saliva is associated with high susceptibility to caries. In rats after the removal of salivary glands a greater incidence of caries on a caries-producing diet is encountered; so that quantity and the physical properties of the saliva would also seem to have some effect [13]; but none of these factors taken individually or together sufficiently explains susceptibility or immunity to caries.

*Structure.*—The effect of nutrition upon the structure of the teeth has been studied by Mellanby [14] and others and a connexion between hypoplasia of the enamel and the calcium-phosphorus and vitamin-D intake has been well demonstrated. The interrelation of these and various other factors in the food such as phytic acid has been shown. The rationale of this work is that the structure of the surface attacked would be expected to be of considerable importance.

A correlation between the caries incidence and the roughness (M. hypoplasia) of the surface of the enamel was shown by Mellanby in London school children [15] and by King [16] in children from various parts of the British Isles. During the years 1929–1947 a reduction of dental caries and hypoplasia was shown in the London school children between the ages of 5 and 6 [15]. The improvement noted is due, it is suggested, to the increased calcifying properties of the diet during pregnancy and the post-natal period, and the reason for the greater increase in improvement noted during 1945–1947 is stated to be clear cut, in that during the whole of the ante-natal and post-natal period calcium had been added to the bread, vitamins to the margarine ration, and milk and cod-liver oil had been available to expectant and nursing mothers. This hypothesis does not explain why Channel Island children [17], left at home on the island, had about half the amount of caries experience of those, who, evacuated to England, were living on our food during the same war period and attained a caries experience identical to that of the English children; nor does it explain why other European countries showed an even greater decrease in caries during the same period; nor why the caries incidence is so low in India where rickets and other deficiency diseases are common.

### *Pre-eruptive Care*

Toverud, K. U., and Toverud, G. [18], have noted the actual effect of pre-eruptive care on children's teeth at their clinic. They compared the children whose parents had received ante-natal and post-natal care, including foods containing an abundance of calcium, phosphorus and vitamin D, with those children who first attended the clinic after the age of 1 year. Both groups received the same post-eruptive care. Although the numbers were not great, comparison of the dental caries experience of the two groups showed that from the age of 2½ to 7 although the dental caries increased year by year, those who received ante-natal and post-natal care had less caries than those who had not. Under the age of 4 years the percentage reduction was marked, but as the caries increased with each year the percentage difference between the two groups became less and less marked. The effect of the treatment was equivalent to a delay in the onset of dental caries of a year or less, but thereafter the number of new cavities per year was imperceptibly affected. Supplementing the food of expectant and nursing mothers therefore may reduce dental caries appreciably during the early years of life, with all the benefits that may mean, but no extravagant claims in the prevention of dental caries by ante-natal care are justifiable, and the effect of supplementing the ration of pregnant and nursing mothers and of children during the war years in England cannot be separated from the effect of other dietary changes during the same period.

Ingestion of fluorine in the drinking water during tooth formation also affects caries incidence. Weaver [4] compared the caries experience of children from North and South

caries experience; but again the yearly increase was scarcely affected and the improvement was equivalent to a delay in onset of from three to five years. In the temporary dentition this makes a vast difference to the clinical picture.

#### *Post-eruptive Nutritional Effects*

Ingestion of fluorine after the tooth has formed is thought to have no effect on caries incidence, but the ingestion of calcium, phosphorus and vitamin D, it is claimed by Mellanby [15], has some effect on the teeth after they are erupted. The post-eruptive effect noted by Mellanby on Institutional children may be due to alteration of the calcium content of the saliva for Patterson found the calcium content of the saliva was doubled after taking the high vitamin diet.

She found that Institutional children had teeth of poor quality but less caries than the Public School and L.C.C. children, and postulated that the Institutional children had a better post-eruptive calcifying diet and therefore became more resistant to caries.

Boyd and Drain [19] brought about an arrest of dental caries and an almost complete cessation of caries incidence in children on a controlled diabetic diet. They consider a balanced diet produces immunity, but the low caries incidence with the high protein diet of the Eskimo and the high cereal diet of the Indian does not bear out this suggestion. It is interesting to note that Boyd and Drain, in balancing the diet, reduced the carbohydrate intake but did not object to refined sugar being taken with meals. Some consider that an ample ingestion of proteins is essential to give protection against caries and cite people living on a high protein diet as evidence for this idea. An adequate supply of vitamin C was at one time thought to reduce caries [20] by 50% but further trials do not support this view. The "quality of the proteins" [21] in fresh, "living" or humus-grown vegetables, although undemonstrated, has been suggested as being the necessary protective agency. Such a factor has not been identified.

Single factors have been used as evidence to support several hypotheses. The fact that Eskimos have a low caries incidence has been used to show that (a) a high protein diet, (b) a diet rich in minerals and vitamin D, (c) a natural diet, (d) a detergent diet, (e) a diet low in carbohydrates, (f) refined carbohydrates, and (g) hard carbohydrates, is the cause of the Eskimo's immunity. The fact is compatible with all of these hypotheses but does not prove any of them.

#### *Local Factors in the Mouth*

The diet also affects the amount and type of food that is left to stagnate about the teeth. After taking a meal of sticky food the stagnation areas can be observed by the presence of food in them, and if a dye is swabbed about the teeth the presence of debris can be more clearly demonstrated. The site, the number and the size of these stagnation areas are shown to depend upon the several factors of mastication habit, the shape of the teeth, and the shape of the fissures upon them and the arrangement and occlusion of the teeth. These areas correspond to the common sites of caries attack and it is natural that attention should be focused on such a clinical correlation. The amount of food left upon the surfaces of the teeth is affected by the physical properties of the food and this aspect has been extensively studied by Sim Wallace [22]. He noted the scouring effect of fibrous foods upon the teeth and the prolonged mastication required when eating them; the combination leaving the teeth clean. With highly refined foods, on the other hand, the scouring effect is missing and mastication is perfunctory, with the result that soft bulky deposits of food are left about the teeth for varying periods of time. Fibrous foods were caught only upon faulty restorations or in abnormal interdental spaces. Bibby [23] found that the chewing of fibrous foods was much superior to the tooth brush in removing particles of various sizes from the mouth.

Price [2] correlated the incidence of dental caries with the refinement of cereals in the diet. When whole grain was utilized caries incidence was low and with increasing degrees of refinement of the grain the caries incidence rose. Price associated this with the removal of phosphorus from the food, but many other substances including fibre are also lost in the refinement of cereals and any effect shown to be due to refinement could be equally ascribed to the loss of any of the substances removed. Bibby [24] also found that the methods of preparation of food, the size of the starch granules and many other factors affected the stickiness of the food and its property of remaining about the teeth.

The factors concerned with the problem of stagnation and its connexion with dental caries include the type of food stagnating about the teeth, the process of its decomposition, the bacteria involved, the end products of decomposition and their possible effect upon the tooth substance, and the various substances present in the mouth.

#### *Miller's Hypothesis*

Miller's supposition [25] to account for what he considered happened was an hypothesis of a two-stage process: an acid decomposition with softening of the tooth substance, consequent upon bacterial fermentation of carbohydrates which lodge after each meal in crevices and between the teeth, followed by a dissolution of the softened tissue which in the case of



enamel was practically wanting. This explanation of the immediate cause of caries has been at different times added to, attacked or confirmed.

In testing [26] the possibility of Miller's acid decalcification hypothesis it is found that the enamel can be dissolved completely, etched, or softened and made opaque by various strengths of acid. Acids have been demonstrated in the mouth by measurements of the pH of the tooth surfaces [27], on material from beneath bacterial plaques [28] and on material from carious cavities. It was shown that a considerable degree of acidity can occur, which, in itself, could produce damage to the tooth surface. Such low readings were only found intermittently but the lowest readings were consistently found in caries-susceptible subjects. It would seem from these observations that dental caries is associated with a considerable degree of acidity which in itself is capable of damaging the tooth structure both *in vivo* and *in vitro*. Teeth are rarely damaged by the acid of fruit juices. Although caries so commonly occurs in an area of stagnation and the soft greenish plaque is associated with enamel destruction beneath it, not all stagnation areas become carious nor is the unhygienic mouth found to be more prone to caries. The type of substance [29] stagnating about the teeth and all the various factors associated with it have been the objects of a great deal of study in seeking the answers to such problems.

*Refined carbohydrates.*—Even before Miller's time sugar was considered bad for the teeth and he and others demonstrated that sugars and starches could be fermented to produce acid by the bacteria of the mouth. Teeth subjected to sugar-saliva and bread-saliva mixtures were attacked as if by acid and the mixture itself became acid. A great many of the steps are now known of fermentation of the carbohydrates to lactic and pyruvic acids [30]. Many of the enzyme systems and co-enzymes involved in the process have been described and the factors which retard or accelerate the process under mouth conditions are known.

The hypothesis that the refined carbohydrates are connected with the cause of dental caries has many points in its favour. Groups of people consuming large quantities of refined carbohydrate show a high caries incidence and when this consumption increases caries incidence increases. Bunting [31] showed that in a small group of Institutional children there was a considerable increase in caries following the addition of sugar to the diet. Bakers and confectioners and those exposed to refined carbohydrate dust suffer from an increased caries incidence in the exposed anterior teeth. People living on an unrefined high carbohydrate diet show a remarkably low incidence in caries, but when this is replaced by more refined carbohydrates the incidence of caries increases [5]. When the consumption of these refined carbohydrates is reduced, such as in wartime, caries incidence is reduced. This has lately been shown to have occurred in Finland, Norway and Denmark [6]. A similar but lesser reduction in caries incidence also occurred in England during the same period and although the total consumption of carbohydrates was increased the refined carbohydrates were reduced. Jay, by reducing the carbohydrate content of the diet (and by increasing the protein content), reduced the incidence of caries in a large number of children. No caries has been produced in animals on diets devoid of carbohydrates [32], and as refined carbohydrates replace whole grain and other foods caries increases considerably. These experiments show many other factors also have an effect. Reduction of food intake without other adjustment to the diet produces a reduction in caries, and feeding the parents on the caries diet before gestation even for two generations increases the incidence [33]. Strain differences are also noted [34].

All such observations allow possibilities and interpretations other than that refined carbohydrates are the dominant factor, but the possibilities have been considerably narrowed down. When the carbohydrate diet, shown to produce caries, is fed to a susceptible strain of animal with addition of specific enzyme inhibitors and without other alteration, the caries incidence is remarkably reduced. Caries can also be similarly reduced by addition of antibiotics. This has been confirmed by clinical observations on human subjects.

The accumulated data would suggest that the intake of refined carbohydrates taken under certain conditions was an important accessory cause of dental caries which cannot be ignored.

#### BACTERIOLOGY

A vast number of different bacteria are commonly present in the mouth and many found in carious cavities are present also on the intact tooth surface. The organism that can withstand the greatest acid concentration is usually found to be *Lactobacillus acidophilus* and for this reason has been the object of much study. Many organisms in pure culture produce acid by the fermentation of carbohydrate but no pure culture of an organism produces acid as rapidly as a mixture of organisms or at the rate that it appears in the mouth. A coccus is usually present in the deepest layer of dental caries; the lactobacillus is only present in a certain percentage of carious areas [35]. Both these organisms, however, are able to produce sufficient acid *in vitro* to damage a tooth surface and both organisms are found in areas upon the teeth where a concentration of acid occurs in the mouth. Both can be present in non-carious mouths but this is not evidence that they do not cause damage under other

circumstances. This may depend on factors such as nutritional supply, the presence of inhibitory agents, and on the presence of other symbiotic or antagonistic bacteria.

Harrison found that of organisms recovered from ground-up carious rat molars, lactobacilli comprised only 0.3% of the total bacteria and streptococci 69%. Plaques studied in carious areas in humans contained lactobacilli in only 51% of cases and streptococci in 92%, in non-carious plaques the lactobacillus was present in 27% and streptococci in 60%. In studying 500 plaques from particular tooth surfaces the *Streptococci viridans* began to decrease forty-two weeks before caries appeared and decreased more rapidly after lesions had developed; the aciduric cocci were present in approximately the same amounts before and after caries commenced, but the lactobacilli showed a steady rise from 12%, in the plaque forty-two weeks before caries started, to 50% after caries had commenced. This observation shows that the presence of the lactobacillus is definitely correlated with the carious process but shows that other organisms also take part. The quantitative presence of the lactobacillus in a sample of saliva is the test widely used for caries susceptibility. The total aciduric organism count, the combined bacterial activity as measured by carbohydrate breakdown, acid production, and solution of calcium in sugar-saliva mixtures, all show a similar correlation with caries activity.

Many types of proteolytic organisms are also present in carious cavities. Burnett [36] isolated over 80 types and although they showed active proteolytic properties on the usual media, none was able to attack dentine or enamel unless it had been first completely decalcified. Pincus [37] has found a proteolytic organism, however, that is capable of attacking the enamel surface. Many organisms in the mouth form pigment, some appear to be associated with caries, but others produce various stains upon the teeth and are associated with a lesser degree of susceptibility. What is certain is that acid is formed rapidly on the tooth surface in the presence of sugar solution [27], and in the caries-susceptible person it is formed more quickly and in greater amounts. This is considered to be almost entirely due to bacterial activity.

*Protective surface membranes.*—Membranes, cuticles and pellicles have been described [38] on the surface of the teeth, originating either from the epithelial remnants of the formative enamel organ or from substances deposited upon the tooth surface. The deposits are shown to be something more than dried mucus. They appear upon abraded and attrition surfaces of the teeth, upon fillings and in fissures, both in the enamel and beside fillings. These membranes are shown to be resistant to acid, but that they have little protective importance is suggested by the fact that they are situated in just those areas which are prone to dental caries.

The protective action of a high fat content of the diet has been noted by many, including Sim Wallace [22], and rats fed on various oils nutritive and inert, mixed with their food, showed [39] a considerable reduction in caries.

#### PROTEOLYSIS

Caries begins on the surface of the enamel. If it does so on an otherwise self-cleansing surface there is deep penetration with little lateral spread, but if it begins on a smooth surface it may spread over that surface in any direction which is so protected as to form a stagnation area [40]. The penetration follows the direction of the prisms and within the enamel substance little lateral spread occurs. In section the lesion forms one or more cones whose bases are upon the surface.

The translucent and glossy surface of the enamel is changed to a dull white opaque area which may map out the interproximal area or follow a course close to the gingival margin as a band, at times surrounding the entire tooth. Instead of the whiteness a pigmentation varying from a light brown to black may take place. This discoloration does not occur in simple acid destruction of enamel. In section this pigmentation shows a distribution somewhat similar to the opaque change. In rapid caries the enamel is chalky white and so is enamel which is being attacked from the dentinal surface, at times over a wide area. This enamel can be scraped away readily by an excavator, leaving the outer surface unchanged.

It has been suggested that the pigmentation indicates a proteolytic change of the organic substance of the enamel [41]. When the apex of the cone of enamel caries touches the dentine at the amelo-dentinal junction and initiates caries of dentine, lateral spread and a more intense colour appear [42]. This increase in speed of the carious process as it reaches dentine and the more intense discoloration are suggested as being due to the greater amount of organic material in dentine and that the carious process is proteolytic in nature [41]. The apex of advancing enamel caries commonly strikes the dentine at an enamel tuft; the earliest changes in the dentine appear immediately beneath it. These enamel tufts contain more organic material than the surrounding enamel, as is shown in decalcified preparations, and, as measured by indentation tests [43], are softer than the surrounding enamel. If the deeper caries of the enamel is proteolytic in nature the whole process might be expected to be similar in nature, including the initial stages. Surface coverings are found on the tooth,

in grooves and in pits and upon the whole tooth surface except in the centre of the self-cleansing areas. These are organic in nature and are present in just those areas in which caries commonly starts. They prove to be resistant to acid and, in fact, act as a protection to acid destruction of the enamel surface in experiments *in vitro* [41]. Structures and faults in the enamel are filled with organic material which was either deposited during formation of the enamel or gained entrance later. These are the lamellæ commonly seen in section. Many pass into an enamel tuft and both tufts and lamellæ are thought by histologists to be of identical nature, i.e. collections of enamel prism sheaths [44]. Many of these lamellæ are full of organisms. Other collections of organisms are found amongst the enamel prisms forming a network, these have been termed pseudo lamellæ [45]. Whether they occur in decalcified areas or are accompanied by decalcification has not been determined.

Consequent upon these findings the hypothesis has been put forward that caries is primarily a proteolytic process and not one of acid decalcification. Frisbie believes the earliest pathological change is an acidophilic alteration of the enamel matrix, indicating a proteolysis of the matrix which is followed by a disorganization of the inorganic constituents. Liquefaction of the matrix frees the less soluble basic tricalcium phosphate and thus favours solution by acidogenic bacteria.

Gottlieb [41] considers that within the substance of the enamel acid decalcification is the spearhead of attack and pigmentation follows, but in lamellæ, which form a ready pathway for organisms direct to the dentine, pigmentation is in advance of the acid attack and that without such lamellæ caries of the enamel would be impossible.

What the clinician understands as caries, Gottlieb observes, starts first as a white chalky area upon a protected surface of the tooth, is produced by acid, penetrates the enamel, then the dentine, and within the substance of the enamel is in advance of the pigmentation. He also states that micro-organisms produce acid as well as a proteolytic enzyme and on several occasions "that caries has two components".

Upon these data there is no justification, except by definition, for him to say that "caries of the dentine as well as of the enamel is entirely a proteolytic action". Preventive measures designed on such a doubtful basis are for that reason not acceptable, but may, nevertheless, be of therapeutic value on another account.

He also states that dentine has about 66% of organic matter and the enamel has only about 5% of organic matter. The figure given by Manly and Deakins [46] for the organic content of dentine is 38.9%. The percentage of 60 to 66% organic material is too great even for percentage by volume; this is of some moment as conclusions are based upon it.

Pincus [47] also suggests that the organic substance in the enamel is of importance in the initiation of caries and found that bacteria exist in the mouth which are capable of attacking enamel without the aid of acid. He found bacteria from carious lesions were able to produce lesions *in vitro* resembling clinical caries without the presence of acid.

He says [48] an explanation of enamel caries may be that enamel protein resembling a mucoprotein may release sulphuric acid by enzymatic hydrolysis through the action of sulphatase which is produced by Gram-negative bacilli commonly present in the mouth. This would result in attack on the relatively insoluble inorganic part of the enamel.

It scarcely seems possible that the small percentage of sulphuric acid that can be derived from the protein, which is itself only present in a small amount in enamel—Anderson [49] gives the figure for enamel protein as 0.3% to 1%—could be capable of destroying the enamel in the manner in which it occurs in enamel caries.

Gottlieb considers that the organic material is increased in the carious area as shown in decalcified sections and that the organic material acts as a barrier against acid attack, protecting the parts beneath. This is brought forward as evidence against acid being the attacking agent in caries, but measurements in the mouth show acid is concentrated in the carious area. This *in vitro* experiment is the exact opposite of what occurs in the mouth; acid is concentrated in the organic material and saliva bathes the surrounding surface.

The pigmentation noted by Gottlieb and others, and suggested as being produced by proteolysis of the small amount of organic material present in enamel, might be produced by secondary invaders from the mouth. He considers the staphylococcus takes part in the causation of dental caries but Matthews [50] can find no such correlation between caries and the presence of a staphylococcus.

Lamellæ run parallel to the long axis of the tooth and where these cross a carious cavity a slight extension of the cavity is seen to run along them, so that they, in fact, are assisting the carious process at this point. They may have been the channels of the introduction of bacteria to the depths of the enamel and so have initiated the carious attack, but many sections of caries of enamel show the apices of the characteristic changes on many occasions do not coincide with lamellæ, nor can the presence of lamellæ explain the cone-shaped penetration, nor the pattern of the attacked enamel surface within a stagnation area. Lamellæ, or faults, in incisor teeth commonly become stained and infected, but do not become carious in length to form narrow vertical cavities resembling fissures in molar cavities.

Events that occur in caries of dentine beneath enamel seem to be of a different order, depending on the different structure, composition and location and have not been included in this account. The initial attack on the enamel surface is the all-important matter in the consideration of preventive measures.

#### BIBLIOGRAPHY

- 1 SHOURIE, K. L. (1947) *J. Amer. dent. Ass.*, 35, 805.
- 2 PRICE, W. A. (1933) *Dent. Digest*, 39, 49.
- 3 COUMOULOS, H., and MELLANBY, M. (1947) *Brit. med. J.* (i), 751.
- 4 WEAVER, R. (1944) *Brit. dent. J.*, 77, 185.
- 5 PEDERSEN, P. O. (1948) *Medd. Grönland*, 142, 3.
- 6 TOVERUD, G. (1949) *Proc. R. Soc. Med.*, 42, 249.
- 7 BODECKER, C. F. (1929) *Dent. Cosmos*, 71, 586.
- 8 ATKINSON, H. F. (1947-8) *Brit. dent. J.*, 83, 10; 84, 6.
- 9 BERGGREN, H. (1947) *Swedish dent. J.*, 40, 18.
- 10 BRODERICK, F. W. (1928) *Dental Medicine*. London.
- 11 HAWKINS, H. (1946) *Practical Pedodontia or Juvenile Operative Dentistry and Public Health Dentistry*. Hogeboom, F. E., Fifth Edition, London.
- 12 GIES, W. J., and ENRIGHT, J. J. (1932) *J. dent. Res.*, 12, 5.
- 13 BIBBY, B. G. (1948) *Oral Surg. Med. Path.*, 2, 72.
- 14 MELLANBY, M. (1934) *Spec. Rep. Ser. med. Res. Council*, No. 191.
- 15 ———, and MELLANBY, H. (1948) *Brit. med. J.* (ii), 409.
- 16 KING, J. D. (1940) *Spec. Rep. Ser. med. Res. Council*, No. 241.
- 17 KNOWLES, E. M. (1946) *Month. Bull. Min. Hlth.*, 5, 162.
- 18 TOVERUD, K. U., and TOVERUD, G. (1945) Report of the First Six Years' Work of the Oslo Health Station for Mothers and Children. Oslo.
- 19 BOYD, J. D., and DRAIN, C. L. (1928) *J. Amer. dent. Ass.*, 15, 1604.
- 20 HANK, M. T. (1929) *J. Amer. dent. Ass.*, 16, 2263.
- 21 HOWARD, A. (1947) *Brit. dent. J.*, 83, 2.
- 22 WALLACE, J. S. (1929) *The Physiology of Oral Hygiene and Recent Research*. London.
- 23 TURESKY, S. S., and BIBBY, B. G. (1944) *J. dent. Res.*, 23, 51.
- 24 BIBBY, B. G. (1935) *J. Amer. dent. Ass.*, 22, 222.
- 25 MILLER, W. D. (1883) *Dent. Cosmos*, 25, 1.
- 26 MCINTOSH, J., JAMES, W. W., and LAZARUS-BARLOW, P. (1922) *Brit. J. exp. Path.*, 3, 138; *Brit. dent. J.*, 43, 728.
- 27 STEPHAN, R. M. (1944) *J. dent. Res.*, 23, 4.
- 28 FOSDICK, L. S., CAMPAIGNE, E. E., and FANCHER, O. E. (1941) *Illinois dent. J.*, 10, 85.
- 29 BUNTING, R. W. (1933) *J. Amer. dent. Ass.*, 20, 773.
- 30 FOSDICK, L. S. (1937) *N.Y. J. Dent.*, 17, 2, 55.
- 31 KOEHLER, M., BUNTING, R. W., and MORRELL, E. (1934) *Amer. J. Dis. Child.*, 48, 6.
- 32 VOLKER, J. F. (1949) *Brit. med. J.* (i), 1000.
- 33 SOGNAES, R. F. (1948) *J. Nutrit.*, 36, 1.
- 34 SHAW, J. H. (1948) *J. Amer. diet. Ass.*, 24, 3.
- 35 HARRISON, R. W. (1948) *J. Amer. dent. Ass.*, 37, 391.
- 36 BURNETT, F. (1948) Personal communication.
- 37 PINCUS, P. (1944) *Brit. dent. J.*, 76, 231.
- 38 VALLOTTON, C. F. (1945) *J. dent. Res.*, 24, 161.
- 39 ROSEBURY, T., and KARSHAN, M. (1939) *J. dent. Res.*, 18, 189.
- 40 KESEL, R. G. (1948) *J. Amer. dent. Ass.*, 37, 4.
- 41 GOTTLIEB, B. (1947) *Dental Caries*. London.
- 42 ———, DIAMOND, M., and APPLEBAUM, E. (1946) *Amer. J. Orthop. oral Surg.*, 32, 6.
- 43 GUSTAFSON, G. (1948) *Odontol. Tidskr.*, 56, 23.
- 44 ——— (1945) *Odontol. Tidskr.*, 53, (Suppl.).
- 45 FRISBIE, H. E., NUCKOLLS, J., and SAUNDERS, J. B. (1944) *J. Amer. Coll. Dentists*, 11, 243.
- 46 MANLY, R. S., and DEAKINS, M. L. (1940) *J. dent. Res.*, 19, 165.
- 47 PINCUS, P. (1939) *Dent. Rec.*, 59, 613.
- 48 ——— (1948) *Nature*, 16, 1014.
- 49 ANDERSON, D. J. (1949) Personal communication.
- 50 MATTHEWS, E., ATKINSON, H. F., SAUNSBURY, P., and CLEGG, H. W. (1949) *Brit. med. J.* (i), 54.

### Birth Conditions and Dental Deformities

By LILAH M. CLINCH, L.D.S. R.C.S.I.

THERE have been many references in the literature to isolated cases of deformities of the jaws caused through difficult labour. In 1946 Gerry and Sangston described the oral conditions of 60 newborn infants, and in 12 of these they found deviated mandibles. Details were given of the types of birth presentation but all deliveries were said to be normal, there was no difficulty in feeding and the deviated mandibles were all corrected spontaneously by the end of the tenth week. Edgar (1933) describes the moulding of the skull in vertex presentations and concludes that "in ordinary cases deformity from moulding disappears in one or two days and in more pronounced cases in two or four days". But Liebreich (1908)

states: "Having studied 2,000 crania in the Anthropological Museum, 3,000 at the Collegio Romano and 400 crania of mummies at the School of Medicine, Cairo—that is to say, crania of different races at different times, even prehistoric—and having compared the results of the studies with the observations on the living of different races, I believe that asymmetry is not a tare, a stigma of malformation, a sign of degeneration, but on the contrary the normal form of the human face." He continues: "I believe the cause of this asymmetry is the last period of foetal life when the pelvis exercises pressure on the embryo's cheek, that is to say, on the left cheek in the commonest form of birth presentation. Thus I conclude that asymmetry is a consequence, a necessary accompaniment of the vertex presentation of the human race and becomes for the human race a distinguishing mark."

This communication is a summary of the results of an examination made by me on 100 children aged between 18 months and 5 years. Detailed histories of the ante-natal and post-natal condition and of the type of presentation were available for all of them.

Of the 100 children examined there were 70 vertex presentations, 20 breech and 10 Caesarean sections. The Queen Charlotte's Textbook of Obstetrics gives the incidence of types of presentations as follows: 96% vertex, 3% breech, 1 in 360 face and 1 in 600 brow.

Colyer has shown cases of gross asymmetry in vertex presentations which he thinks are due to injury during delivery but he considers the cases most likely to show deformities are breech, face and brow presentations. At the Perivale Maternity Hospital where I obtained my material I was unable to find any cases of face or brow presentation which could be followed up. But I selected 20 breech cases and 10 Caesarean sections, hence the large percentage of these types in my cases.

Of the 70 vertex cases examined by me 38 were left occiput anterior, 28 right occiput anterior, 2 right occiput posterior and 2 left occiput posterior. Of the 38 cases of left occiput anterior 9 showed slight flattening on the left side of the maxillary arch and 1 showed slight flattening on the right. Of the 28 cases of right occiput anterior, 5 showed slight flattening on the right and 2 on the left. Both cases of right occiput posterior showed flattening, one on the left and one on the right. One of the 2 cases of left occiput posterior showed flattening on the left. In the 70 vertex cases there were therefore 20 cases showing asymmetry. Most of these asymmetries were demonstrable only by means of a symmetroscope. There were also 2 cases which showed obvious flattening of the head but no asymmetry of the dental arches.

In breech presentations the delivery of the after-coming head is sometimes carried out by jaw and shoulder traction. The index finger of one hand is placed inside the mouth so as to obtain a grip on the lower jaw, the fingers of the other hand being used to grasp the shoulders from behind. Considerable force is sometimes used in this manoeuvre and cases have been reported of fracture of the mandible. Of the 20 breech cases, 4 showed flattening on the left side of the dental arches, 3 of these were more obvious than most of the asymmetries in the vertex cases.

Of the 10 Caesarean sections one showed slight flattening on the left side of the dental arches, and one showed obvious asymmetry of the head but no asymmetry of the dental arches.

It was very interesting to note the high incidence of malocclusion of the deciduous dentition among these children. Of the 100 children examined only 32 had normal occlusion. There were 36 cases of postnormal occlusion of the mandible, 19 cases of normal antero-posterior arch relationship associated with close or open bite or imbrication of the teeth, 7 cases of prenormal occlusion of the mandible and 6 cases of prenormal maxilla. 22 children were finger or thumb suckers, and of these 12 had postnormal mandibles, 2 prenormal mandibles, 4 a unilateral prenormal maxilla and 4 had normal antero-posterior arch relationship with open bite and displacement of the incisor teeth.

No case of normal occlusion was associated with a sucking habit. But even if every case caused by a habit could overcome the malformation when the habit ended there would still only be 54 cases of normal occlusion out of 100. This is a considerably lower proportion than is found in the mixed or permanent dentitions and it would seem likely that many of these early malocclusions are cases of delayed growth which may cause a temporary disproportion between the upper and lower jaws.

#### SUMMARY

- (1) Of 100 cases, 25 showed slight asymmetry of the dental arches. There seems little indication that the asymmetry is connected with the type of birth presentation.
- (2) Of the 100 cases examined only 32 had normal occlusion.
- (3) 22 children were finger or thumb suckers and no case of normal occlusion was associated with a sucking habit.

#### BIBLIOGRAPHY

- COLYER, J. F. (1942) *Trans. Brit. Soc. Study Orthodont.*, 39.  
 EDGAR, J. C. (1933) *Practice of Obstetrics*. Sixth Edition, p. 303. London.  
 GERRY, R. G. and SANGSTON, R. E. (1946) *Amer. J. Oral Surg.*, 32, 439.  
 LIEBREICH, R. (1908) *L'Asymétrie de la Figure et son Origine*. Paris.

# Section of Epidemiology and State Medicine

President—Sir ALLEN DALRY, M.D., F.R.C.P., D.P.H., K.H.P.

[JUNE 3, 1949]

## DISCUSSION: HOW TO WRITE A REPORT. [Abstract]

**Dr. C. Leonard Williams:** The would-be writer should begin by first of all examining himself to discover what manner of man he is; thus he may hope to learn his best means of expression. The easiest way of classifying people is by noting what manner of speaker each person is, because the art of expression or writing is nothing other than a development and a modification of speech. There is the guided orator with the ability "the applause of listening Senates to command"; there is the class teacher who has his counterpart in the witty conversationalist at the dinner table, and last of all there is the speaker who is all but dumb, save only in an audience of one.

The gifted parliamentarian who, in these periods, enchants the ears of his delighted audience, and the speaker who looks for the plaudits of the crowd are alike in this—that they both depend upon rapport. The cheerleaders of the Senate House are necessary to the parliamentarian because this applause is an indication and a measure of rapport. In the same way the roars of the crowd are essential to the mob orator. It is therefore only natural that these men are tempted to write as though applause were just round the corner.

There will never be a very high level of scientific or academic material put forth by such writers, because their manner of speaking and writing would in fact appeal to a very large audience, the highest common factor among which would of necessity be relatively low.

It is to the brilliant class teacher that people have to look for other scientific treatises which appeal to a very small reading public.

The man who is not a conversationalist save only in an audience of one is the least predictable of the three classes of speakers; there has been a sufficient number of able writers who have been morose, so far as social conversation is concerned, but who, nevertheless, could be brilliant in literature. Generally speaking, this last class of speaker achieves his best literary efforts in personal letters, and oftentimes in public reports there has been found a brilliant letter of introduction followed by a report which was altogether disappointing. It seems a pity that these people do not go on writing a series of letters when, I feel quite sure, they would achieve distinction.

Revision and recasting of a paper or article are essential for even the most experienced author. There is no art of writing as such, and a writer who has not got a message to deliver to the reader is just as impossible as an evangelist without a gospel.

Finally I shall mention briefly some points of practical interest and importance, such as the need for short paragraphs, short sentences and short words. All statistics should be omitted, save only those that are essential to the understanding of the text. Then there is the need to study the galley proof very carefully—a precaution too often left to the printer's reader. Every illustration should be looked upon as a picture on a wall and placed on the page with the same care and finish.

Many readers find a difficulty in interpreting graphs, and never more than two curves should be shown on the reproduction of any one graph.

Those who know their subject well can soon master the technique of production. Medical subjects should be written clearly and simply, and the author must always bear in mind that the arguments and deductions may not be readily followed by the reader—however learned—who is not also a worker in the medical field.

**Professor A. Bradford Hill:** In scientific papers and reports the basic statistical data should be set out in tables as fully as possible. Medical writers, and readers, usually prefer diagrams and find (or think they find) them easier to read than tables. Properly drawn they certainly can assist in the interpretation of numerical data but they can, also, be most misleading and, indeed, usually require just as much careful study by the reader as do statistical tables. Graphs should, therefore, be regarded only as an extra aid to interpretation and not as a substitute for the numerical data which comprise the fundamental evidence. This statistical evidence, also, should not, as a rule, be relegated to an appendix. If it forms the basis of the argument put forward by the author, then the reader must be expected to consider it in relation to that argument and not to accept it lightly without consideration or to take it on trust. Readers who are prepared to do that can skip the tables, those who are not, should be given the statistics in their proper place and not have to hunt for them at the end of the report.

In reporting rates or percentages it is important to give the size of the experience underlying them. A fatality rate of 50% obviously has a very different meaning when it is derived from 6 patients of whom 3 died than when it comes from 60 of whom 30 died. Medical writers often leave such facts out, more through lack of appreciation of their importance rather than deliberately—as is often done in propaganda or in advertisements. Without such evidence the statistical argument is always suspect and frequently should be rejected entirely.

Too often, also, the basic data are compressed into an average value—as for instance in a recently reported portrait of the average Congressman in the U.S.A. which showed him to be 5 feet 9 inches in height, 184 lb. in weight, as having two children and a bit, and three-quarters of a college diploma! But such averages are hardly more foolish or less informative than many of the corresponding values published in medical and scientific papers. The average entirely ignores, of course, the essential variability of a series of measurements. But if the measurements do not vary there is no average to calculate, if they do vary that variability cannot be neglected. It is not often possible, or even indeed desirable, to publish the whole of the original protocols but the rule to follow is to give, as fully as possible, the frequency distributions constructed from the data. Those distributions give, in brief, most of the information at the writer's disposal and upon which his calculations and arguments were based.

Medical workers are now fully aware of the importance of following up *all* patients in, say, an inquiry into the upshot of a form of treatment, or of getting answers from *all* persons approached for some or other information. Without response from all such persons the answers may form a very unrepresentative sample. It is, however, perhaps, not sufficiently realized how important it is to state the proportion actually traced or answering. Without that figure the inquiry cannot be critically appraised. If the "lost-sight-of" or "won't-answer" rate is high the results must be looked at askance, if it be low no great error can be present. The reader is entitled to be told. To-day, also, many inquiries depend upon sampling, some specific procedure for drawing the sample being adopted. The details of that procedure should always be set out in a report. Whether the sample is likely or no to be representative of the "universe" from which it was drawn depends upon that statistical procedure and how successfully it was applied. Again, the reader should be informed and enabled to draw his own conclusions.

In drawing conclusions from statistical tables it is important to see that those conclusions, and quoted figures, are in accordance with the figures given in the tables. The number of occasions on which text and table do not agree in published papers is astonishingly high so that either the reader is misled or, through observing these simple mistakes, encouraged seriously to doubt the author's competence. Precision in presenting statistics is, in fact, the fundamental—precision in defining carefully and exactly by efficient headings what a table contains; precision in stating fully the basis of the proportions and rates therein; precision in clear statements of the nature of the data, e.g. that patients dying within twenty-four hours of treatment were not included in the statistics; and precision in accuracy of quotation and in statement of the statistical methodology applied, e.g. in drawing a sample. Statistics at the best of times lend themselves, even without intention, to misleading comparisons; every effort should be made through accuracy of statement not to increase those risks unnecessarily.

[April 4, 1949]

## DISCUSSION ON IMMUNITY RESPONSES IN THE YOUNG WITH SPECIAL REFERENCE TO DIPHTHERIA

### Dr. H. J. Parish: *Diphtheria: Immunity of Adult Populations*

Contrary to a belief still widely held, infants do not necessarily receive from their parents a useful degree of immunity to diphtheria. The impression which has persisted from early work by Park and Zingher, and also Schick, in the U.S.A., is that approximately 85 to 90% of mothers are immune. However, Wright and Clark (1944) mention 42.4% of Schick-negative adults in a London suburb, and Stott (1946) 38.2% in a country district of Sussex; some of the recent Scandinavian figures are even lower. The factors responsible for these percentages are the density of the population, and the amount of natural and artificial immunization in each area. Many infants in different countries are insufficiently protected at birth.

*Diphtheria cases under 1 year of age.*—Diphtheria cases in the first year of life are not as rare as is sometimes thought. Murray (1943) in South Africa found that 102 (4.5%) of 2,237 cases were in this age-group; 20 of these were aged 0-6 months. Liakka (1947) in Finland reported 46 cases (5%) in the first year out of a total of 921; 31 were in the newborn,

with 9 deaths. Several local epidemics in neonatal and nursing infants have also been reported from Norway and Sweden with fatality rates of the order of 20%. Many cases in the newborn are nasal diphtheria and the diagnosis tends to be missed, infants often being ill for one week or more before the nature of the infection is realized. In Great Britain, where the diphtheria case incidence and mortality have declined so markedly during recent years, the provisional figures (6 deaths in 1948) for the first year of life show that at present no problem exists. However, the situation must be watched in connexion with the amount of immunization and of carriage of diphtheria in the country generally.

*Immunity and immunizability of infants.*—Two current beliefs regarding the immunity and immunizability of young infants should be examined critically. The first is that an adequate degree of temporary immunity is derived from the mother. As we have just seen, this is untrue in many areas. Further, apart from any question of immunity, there may be less diphtheria in the early months of life because infants are less exposed to infection than older children. Another factor in the evidence may be that the mucous membranes of young babies are more "resistant" than older children, the belief that the young infant is immune was probably much influenced by the results of Schick tests; evidence from Schick readings in the early months of life may have been misinterpreted, for we now know that many infants are Schick-negative without having adequate antitoxin in their serum.

The second common belief to be examined is that the antibody-producing mechanism is poorly developed below 6 months. This is untrue. Would not older children, like older horses, be expected to respond better than the young, owing to the possible presence of basal immunity in their serum, from the steady sub-infecting doses of toxigenic bacilli? The responses of young infants may also be "blanketed" by inherited antibody from their mothers. When passive antibody is present, does it follow that the infants' cells are so undeveloped that they are incapable of antibody production? It will be shown later in this Discussion that infants' cells can respond well to specific stimuli.

*Transmission of antibodies (actively acquired) from mother to offspring.*—Antibodies which the mother has herself acquired actively are passed on to her offspring by the placenta (mainly) and by the colostrum. The former route is used by man and rodents, such as the rabbit and guinea-pig. In man the gamma globulin is as high in the serum of the newborn as in the maternal serum, and the concentration of antibodies is just as high. Transmission of immunity via the colostrum is the method in calves, foals, lambs, kids and pigs; in the case of some of these animal species it is known that there is no gamma globulin in the serum of the newborn. Antibody is obtained by the young animal through the alimentary tract, which has high absorptive power and no digestive ferments.

*Antibodies in colostrum and milk.*—Colostrum (including human) contains a higher concentration of globulin than the later milk. Before or immediately after birth the colostrum titre approaches and may greatly exceed the serum titre of the mother; this applies not only to antitoxins but to other antibodies such as typhoid agglutinins. Later, the titre falls rapidly (Mason, Dalling and Gordon, 1930, and Sugg, 1935). One can conclude that colostrum and milk play a negligible role in humans in transmitting antitoxic immunity in early life, although later the mature milk may have something to do with the maintenance of the early protection acquired via the placenta.

*Schick tests in young infants.*—It is interesting and instructive to consider typical data of the use of the Schick test in mothers and young infants. Wright and Clark (1946) reviewed five groups of figures from the literature. In 171 comparisons, both mothers and infants were Schick-positive. In a further 99 comparisons there was a discrepancy, the mothers being positive and the infants negative. Thus, there was "anergy" or complete failure to respond in more than one-third of the infants of Schick-positive mothers. With reference to the 171 agreements, the positive reactions of the newborn infants were usually weaker and more transient than those of the mothers. The infant's skin is obviously less responsive to Schick toxin, as it is to certain other irritants, such as scarlet fever (erythrogenic) toxin, quinine, turpentine, iodoform and ultraviolet light. Under the microscope the cutaneous blood-vessels are relatively rich and superficial in infants, so that a probable factor in the weaker responses is the more prompt removal of the Schick toxin, &c., from the site of injection (Wright and Clark, 1946).

*Schick tests in infants over 6 months old.*—Infants over 6 months of age are usually, but not always, Schick-positive. For example, Stott (1946) found 4 of 38 babies aged 10 to 12 months Schick-negative, and 2 of 8 babies aged 6 to 9 months negative. It is uncertain whether the immunity of these babies was passive or active in origin, but it is safe to assume that the percentage of Schick-negative babies over 6 months old will increase in well-immunized communities. This point is discussed by subsequent speakers.

*Immunity responses in whooping cough.*—Finally, although diphtheria is not a serious disease at present in the first 6 months of life, whooping cough has at this age-period both a high incidence and a high fatality rate. Evidence (for what it is worth) from the titration



of agglutinins in mothers and babies would suggest that passive immunity to this dread infection cannot be expected with regularity in the newborn. With regard to active immunization with vaccine some American workers, including Waddell and L'Engle (1946), regard this procedure as safe and practicable within the first 3 months of life, although success is not possible in all infants. Research on this important point is still in progress. Other speakers in this Discussion will show that with proper safeguards immunization against diphtheria is possible some months before the eighth month—the time recommended officially at present for the first dose of the course. As our knowledge increases, it may be possible to use with confidence a combined prophylactic for both diphtheria and whooping cough at the fourth month or even earlier.

#### REFERENCES

- LIAKKA, V. (1947) *Ann. Med. intern. Fenn.*, 36, 584.  
 MASON, J. H., DALLING, T., and GORDON, W. S. (1930) *J. Path. Bact.*, 33, 783.  
 MURRAY, N. L. (1943) *S.A. med. J.*, 17, 334.  
 STOTT, W. B. (1946) *Ann. Rep. M.O.H.* Cuckfield R.D. (see *Medical Officer* (1947) 78, 41).  
 SUGG, J. V. (1935) *Amer. J. Hyg.*, 22, 227.  
 WADDELL, W. W., and L'ENGLE, C. S. (1946) *J. Pediat.*, 29, 487.  
 WRIGHT, G. P., and CLARK, W. M. (1944) *Brit. med. J.* (ii), 146.  
 ———, ——— (1946) *Clin. Sci.*, 6, 13.

#### Miss M. Barr: *Immunization of Young Lambs.*

An experiment was carried out, in collaboration with Dr. J. W. Howie during the 1948 lambing season, to determine the effect of antitoxin, passively conferred via colostrum, upon active immunization of young lambs.

In order to eliminate possible complications arising during the experiment as a result of natural infection, diphtheria A.P.T. was used as antigen. By varying the times of injections of groups of pregnant ewes, a very wide range (0.004 to 15 units/ml.) of passive antitoxin was circulating in the lambs when active immunization was started.

As we were specially interested in the protection of lambs during the first 8 weeks of life, their active immunization was started at the age of 2 weeks, a second dose of A.P.T. being given four weeks later. Blood samples for antitoxin titrations were taken at the time of the first and second injections and ten days after the second injection. It was found that only one lamb out of 30 whose passive antitoxic value was 0.3 unit/ml. or higher at the time of the first injection, responded actively during the four weeks following this injection, though all lambs whose passive value lay between 0.3 and 1.5 units developed good basal immunity. All the animals with initially 1.5 units or less gave a good response within ten days of the second injection, but 9 of the 15 lambs with 2 or more units failed to produce any active antitoxin, though some of them had given an intermediate response seven weeks later.

Those lambs which had a passive value of 0.15 unit or lower when 2 weeks old produced as much active antitoxin (over 7 units/ml.) as parent ewes fed on ordinary pasture. In an earlier experiment groups of lambs were given a first injection of A.P.T. at birth: there was no passive antitoxin present. Lower values (2.8 units) were produced following two injections, at birth and 4 weeks, or three injections, birth, 2 and 4 weeks. Although the values of these two groups were the same at 4 weeks and 10 days, some advantage was gained by the inclusion of an injection at 2 weeks old, because at the age of 3 weeks these lambs had a value of 1.19 units as compared with 0.12 unit for the controls.

It is hoped, by using the requisite antigens, to use the information obtained in this experiment in working out methods of protecting young lambs against lamb dysentery and pulpy kidney.

#### Dr. K. J. Randall: *Immunization of Infants.*

The work I shall now describe has been carried out during the past two and a half years at Salomon's Welfare Centre, Guy's Hospital, and St. Alfege's Hospital, Greenwich, in co-operation with the Wellcome Research Laboratories where all the antitoxin titrations have been performed.

Our aim has been to investigate the immunity response to A.P.T. of infants at varying ages. There appear to be two important factors influencing this response which we had to investigate, namely: (1) The circulating passive antitoxin present at the time of the first injection, and (2) the age of the baby at this time.

In order to gain some information about the circulating antitoxin we Schick-tested 71 expectant mothers at the 4th month of pregnancy, and immunized those who were Schick-positive with 2 doses of A.P.T. at an interval of two months. Bleedings were then taken from all the mothers a few weeks before delivery. Antitoxin estimations were performed by Mr. Glenny and Miss Barr on these specimens, on cord blood samples, and on blood

samples taken from the infants at intervals of about two months. The children were bled by heel-prick using a special scoop designed by Mr. F. Tottem, which is detachable from the 3 by  $\frac{1}{2}$ " tube on which it is used, and is easily sterilized by boiling. The tubes contain potassium oxalate in solution, and the antitoxin in the plasma is estimated. We have, so far, taken over 190 bleedings from infants in the course of this investigation.

Mr. Glenny will give details of the gradual loss of passive antitoxin from the blood of these infants. The great majority had less than 0.005 unit (i.e. were below the Schick level) by the time they were 6 months of age. However, when there were high initial levels in the cord blood, some of the children retained their immunity for far longer periods. For example, in one case, with 120 units per ml in the cord blood 0.2 unit was still present when the child was 11 $\frac{1}{2}$  months old.

As the result of this series of estimations, we have available a chart from which the passive antitoxin present at any age up to 1 year can be calculated if the level in the cord blood is known.

We then immunized a number of babies of varying ages and with different amounts of passive antitoxin at the time of the first injection, in order to study the importance of these two factors.

The results so far investigated show that:

First, with regard to age, infants immunized in the 2-4 months age-group have responded as well as those over 6 months. Incidentally, 3 of the children were exactly 8 weeks old at the time of their first injection.

Secondly, with reference to the influence of passive antitoxin on the response, all except 2 of those shown on the main chart had less than 0.05 unit and the responses were generally good. Of the 3 children who possessed 0.05 unit one responded very well producing 1 unit six weeks later, and the other two produced 0.1 and 0.01 unit respectively.

Three infants with 0.1 unit and one with 0.2 unit all failed to respond.

We have also given 6 children their first injection at birth. One of these infants who had 0.04 unit before injection showed a slight response. Unfortunately, 4 of the remainder had 0.1, 0.2, 0.5, and 0.5 unit respectively in the cord blood specimens, and as expected, there was no antitoxin response. The sixth child in this group had less than 0.01 unit in the cord sample, and despite two injections of A.P.T. at birth and at 2 months, no detectable antitoxin was found in later bleedings. As the mother of this child was herself immunized during pregnancy and failed to respond, this suggests another factor which may influence the immunity response, namely, an inherited inability of the infant to produce certain antibodies.

These results suggest two very important conclusions:

(1) That infants of 2 months and probably less, injected with A.P.T., will produce diphtheria antitoxin as well as those over 6 months.

(2) That a reasonable response may be expected provided there is not more than 0.05 unit of passive antitoxin present at the time of the first injection with 0.5 ml. A.P.T.

The number of infants so far investigated is small but in view of the results already obtained we are now immunizing a large number of babies during the first 3 months of life. I would like to say that the injection of babies under 4 months is far less upsetting to the child, and a more rapid procedure than when it is performed at the age of 9 months or later.

In order to get some idea of the immunity of the population at the present day, we have tested two random sets of 100 cord samples from Guy's and St. Alfege's Hospitals respectively. Although, in the main, these results are comparable, there were 5% more below Schick level in the St. Alfege's series. This difference in two similar social districts is interesting, but probably of no importance if examined statistically. These figures show that the percentage of non-immune females in these two districts is between 25 and 30% at the present day.

One further interesting feature has been revealed by the testing of these cord samples: if the 50 samples from the original mothers who were Schick-tested and found to be negative are compared with 50 controls (not Schick-tested) from the same district but with serum antitoxic values above the Schick level, the lowest recorded value in those who were Schick-tested was 0.04 unit with an average for the 50 women of 0.776 unit. The average for the controls with 0.01 unit or more was 0.203 unit. Thus, treating the two populations as immunologically similar, 50 Schick-negative women gained an average of at least 0.5 unit over those women not injected with the Schick dose of toxin. In actual fact, the gain must have been even greater as the Schick test in most cases was performed at least four months before delivery; with the lapse of time the antitoxic level may have passed its peak. Also, 23 of those who were Schick-tested had cord bloods of 1 unit or more, whereas only 4 in the control group reached these values. Mr. Glenny will discuss the significance of these findings.

The secretion of diphtheria antitoxin in colostrum and milk has also been investigated

of agglutinins in mothers and babies would suggest that passive immunity to this dread infection cannot be expected with regularity in the newborn. With regard to active immunization with vaccine some American workers, including Waddell and L'Engle (1946), regard this procedure as safe and practicable within the first 3 months of life, although success is not possible in all infants. Research on this important point is still in progress. Other speakers in this Discussion will show that with proper safeguards immunization against diphtheria is possible some months before the eighth month—the time recommended officially at present for the first dose of the course. As our knowledge increases, it may be possible to use with confidence a combined prophylactic for both diphtheria and whooping cough at the fourth month or even earlier.

#### REFERENCES

- LIAKKA, V. (1947) *Ann. Med. intern. Fenn.*, 36, 584.  
 MASON, J. H., DALLING, T., and GORDON, W. S. (1930) *J. Path. Bact.*, 33, 783.  
 MURRAY, N. L. (1943) *S.A. med. J.*, 17, 334.  
 STOTT, W. B. (1946) *Ann. Rep. M.O.H. Cuckfield R.D.* (see *Medical Officer* (1947) 78, 41).  
 SUGG, J. V. (1935) *Amer. J. Hyg.*, 22, 227.  
 WADDELL, W. W., and L'ENGLE, C. S. (1946) *J. Pediat.*, 29, 487.  
 WRIGHT, G. P., and CLARK, W. M. (1944) *Brit. med. J.* (ii), 146.  
 —, — (1946) *Clin. Sci.*, 6, 13.

#### Miss M. Barr: Immunization of Young Lambs.

An experiment was carried out, in collaboration with Dr. J. W. Howie during the 1948 lambing season, to determine the effect of antitoxin, passively conferred via colostrum, upon active immunization of young lambs.

In order to eliminate possible complications arising during the experiment as a result of natural infection, diphtheria A.P.T. was used as antigen. By varying the times of injections of groups of pregnant ewes, a very wide range (0.004 to 15 units/ml.) of passive antitoxin was circulating in the lambs when active immunization was started.

As we were specially interested in the protection of lambs during the first 8 weeks of life, their active immunization was started at the age of 2 weeks, a second dose of A.P.T. being given four weeks later. Blood samples for antitoxin titrations were taken at the time of the first and second injections and ten days after the second injection. It was found that only one lamb out of 30 whose passive antitoxic value was 0.3 unit/ml. or higher at the time of the first injection, responded actively during the four weeks following this injection, though all lambs whose passive value lay between 0.3 and 1.5 units developed good basal immunity. All the animals with initially 1.5 units or less gave a good response within ten days of the second injection, but 9 of the 15 lambs with 2 or more units failed to produce any active antitoxin, though some of them had given an intermediate response seven weeks later.

Those lambs which had a passive value of 0.15 unit or lower when 2 weeks old produced as much active antitoxin (over 7 units/ml.) as parent ewes fed on ordinary pasture. In an earlier experiment groups of lambs were given a first injection of A.P.T. at birth: there was no passive antitoxin present. Lower values (2.8 units) were produced following two injections, at birth and 4 weeks, or three injections, birth, 2 and 4 weeks. Although the values of these two groups were the same at 4 weeks and 10 days, some advantage was gained by the inclusion of an injection at 2 weeks old, because at the age of 3 weeks these lambs had a value of 1.19 units as compared with 0.12 unit for the controls.

It is hoped, by using the requisite antigens, to use the information obtained in this experiment in working out methods of protecting young lambs against lamb dysentery and pulpy kidney.

#### Dr. K. J. Randall: Immunization of Infants.

The work I shall now describe has been carried out during the past two and a half years at Salomon's Welfare Centre, Guy's Hospital, and St. Alfege's Hospital, Greenwich, in co-operation with the Wellcome Research Laboratories where all the antitoxin titrations have been performed.

Our aim has been to investigate the immunity response to A.P.T. of infants at varying ages. There appear to be two important factors influencing this response which we had to investigate, namely: (1) The circulating passive antitoxin present at the time of the first injection, and (2) the age of the baby at this time.

In order to gain some information about the circulating antitoxin we Schick-tested 71 expectant mothers at the 4th month of pregnancy, and immunized those who were Schick-positive with 2 doses of A.P.T. at an interval of two months. Bleedings were then taken from all the mothers a few weeks before delivery. Antitoxin estimations were performed by Mr. Glenny and Miss Barr on these specimens, on cord blood samples, and on blood

samples taken from the infants at intervals of about two months. The children were bled by heel-prick using a special scoop designed by Mr. F. Tottem, which is detachable from the 3 by  $\frac{3}{8}$ " tube on which it is used, and is easily sterilized by boiling. The tubes contain potassium oxalate in solution, and the antitoxin in the plasma is estimated. We have, so far, taken over 190 bleedings from infants in the course of this investigation.

Mr. Glenn will give details of the gradual loss of passive antitoxin from the blood of these infants. The great majority had less than 0.005 unit (i.e. were below the Schick level) by the time they were 6 months of age. However, when there were high initial levels in the cord blood, some of the children retained their immunity for far longer periods. For example, in one case, with 120 units per unit in the cord blood 0.2 unit was still present when the child was 114 months old.

As the result of this series of estimations we have available a chart from which the passive antitoxin present at any age up to 1 year can be calculated if the level in the cord blood is known.

We then immunized a number of babies of varying ages and with different amounts of passive antitoxin at the time of the first injection, in order to study the importance of these two factors.

The results so far investigated show that:

First, with regard to age, infants immunized in the 2-4 months age-group have responded as well as those over 6 months. Incidentally, 3 of the children were exactly 8 weeks old at the time of their first injection.

Secondly, with reference to the influence of passive antitoxin on the response, all except 2 of those shown on the main chart had less than 0.05 unit and the responses were generally good. Of the 3 children who possessed 0.05 unit one responded very well producing 1 unit six weeks later, and the other two produced 0.1 and 0.01 unit respectively.

Three infants with 0.1 unit and one with 0.2 unit all failed to respond.

We have also given 6 children their first injection at birth. One of these infants who had 0.04 unit before injection showed a slight response. Unfortunately, 4 of the remainder had 0.1, 0.2, 0.5, and 0.5 unit respectively in the cord blood specimens, and as expected, there was no antitoxin response. The sixth child in this group had less than 0.01 unit in the cord sample, and despite two injections of A.P.T. at birth and at 2 months, no detectable antitoxin was found in later bleedings. As the mother of this child was herself immunized during pregnancy and failed to respond, this suggests another factor which may influence the immunity response, namely, an inherited inability of the infant to produce certain antibodies.

These results suggest two very important conclusions:

(1) That infants of 2 months and probably less, injected with A.P.T., will produce diphtheria antitoxin as well as those over 6 months.

(2) That a reasonable response may be expected provided there is not more than 0.05 unit of passive antitoxin present at the time of the first injection with 0.5 ml. A.P.T.

The number of infants so far investigated is small but in view of the results already obtained we are now immunizing a large number of babies during the first 3 months of life. I would like to say that the injection of babies under 4 months is far less upsetting to the child, and a more rapid procedure than when it is performed at the age of 9 months or later.

In order to get some idea of the immunity of the population at the present day, we have tested two random sets of 100 cord samples from Guy's and St. Alfege's Hospitals respectively. Although, in the main, these results are comparable, there were 5% more below Schick level in the St. Alfege's series. This difference in two similar social districts is interesting, but probably of no importance if examined statistically. These figures show that the percentage of non-immune females in these two districts is between 25 and 30% at the present day.

One further interesting feature has been revealed by the testing of these cord samples: if the 50 samples from the original mothers who were Schick-tested and found to be negative are compared with 50 controls (not Schick-tested) from the same district but with serum antitoxic values above the Schick level, the lowest recorded value in those who were Schick-tested was 0.04 unit with an average for the 50 women of 0.776 unit. The average for the controls with 0.01 unit or more was 0.203 unit. Thus, treating the two populations as immunologically similar, 50 Schick-negative women gained an average of at least 0.5 unit over those women not injected with the Schick dose of toxin. In actual fact, the gain must have been even greater as the Schick test in most cases was performed at least four months before delivery; with the lapse of time the antitoxic level may have passed its peak. Also, 23 of those who were Schick-tested had cord bloods of 1 unit or more, whereas only 4 in the control group reached these values. Mr. Glenn will discuss the significance of these findings.

The secretion of diphtheria antitoxin in colostrum and milk has also been investigated

of agglutinins in mothers and babies would suggest that passive immunity to this dread infection cannot be expected with regularity in the newborn. With regard to active immunization with vaccine some American workers, including Waddell and L'Engle (1946), regard this procedure as safe and practicable within the first 3 months of life, although success is not possible in all infants. Research on this important point is still in progress. Other speakers in this Discussion will show that with proper safeguards immunization against diphtheria is possible some months before the eighth month—the time recommended officially at present for the first dose of the course. As our knowledge increases, it may be possible to use with confidence a combined prophylactic for both diphtheria and whooping cough at the fourth month or even earlier.

## REFERENCES

- LIAKKA, V. (1947) *Ann. Med. intern. Fenn.*, 36, 584.  
 MASON, J. H., DALLING, T., and GORDON, W. S. (1930) *J. Path. Bact.*, 33, 783.  
 MURRAY, N. L. (1943) *S.A. med. J.*, 17, 334.  
 STOTT, W. B. (1946) *Ann. Rep. M.O.H.* Cuckfield R.D. (see *Medical Officer* (1947) 78, 41).  
 SUGG, J. V. (1935) *Amer. J. Hyg.*, 22, 227.  
 WADDELL, W. W., and L'ENGLE, C. S. (1946) *J. Pediat.*, 29, 487.  
 WRIGHT, G. P., and CLARK, W. M. (1944) *Brit. med. J.* (ii), 146.  
 —, — (1946) *Clin. Sci.*, 6, 13.

Miss M. Barr: *Immunization of Young Lambs.*

An experiment was carried out, in collaboration with Dr. J. W. Howie during the 1948 lambing season, to determine the effect of antitoxin, passively conferred via colostrum, upon active immunization of young lambs.

In order to eliminate possible complications arising during the experiment as a result of natural infection, diphtheria A.P.T. was used as antigen. By varying the times of injections of groups of pregnant ewes, a very wide range (0.004 to 15 units/ml.) of passive antitoxin was circulating in the lambs when active immunization was started.

As we were specially interested in the protection of lambs during the first 8 weeks of life, their active immunization was started at the age of 2 weeks, a second dose of A.P.T. being given four weeks later. Blood samples for antitoxin titrations were taken at the time of the first and second injections and ten days after the second injection. It was found that only one lamb out of 30 whose passive antitoxic value was 0.3 unit/ml. or higher at the time of the first injection, responded actively during the four weeks following this injection, though all lambs whose passive value lay between 0.3 and 1.5 units developed good basal immunity. All the animals with initially 1.5 units or less gave a good response within ten days of the second injection, but 9 of the 15 lambs with 2 or more units failed to produce any active antitoxin, though some of them had given an intermediate response seven weeks later.

Those lambs which had a passive value of 0.15 unit or lower when 2 weeks old produced as much active antitoxin (over 7 units/ml.) as parent ewes fed on ordinary pasture. In an earlier experiment groups of lambs were given a first injection of A.P.T. at birth: there was no passive antitoxin present. Lower values (2.8 units) were produced following two injections, at birth and 4 weeks, or three injections, birth, 2 and 4 weeks. Although the values of these two groups were the same at 4 weeks and 10 days, some advantage was gained by the inclusion of an injection at 2 weeks old, because at the age of 3 weeks these lambs had a value of 1.19 units as compared with 0.12 unit for the controls.

It is hoped, by using the requisite antigens, to use the information obtained in this experiment in working out methods of protecting young lambs against lamb dysentery and pulpy kidney.

Dr. K. J. Randall: *Immunization of Infants.*

The work I shall now describe has been carried out during the past two and a half years at Salomon's Welfare Centre, Guy's Hospital, and St. Alfege's Hospital, Greenwich, in co-operation with the Wellcome Research Laboratories where all the antitoxin titrations have been performed.

Our aim has been to investigate the immunity response to A.P.T. of infants at varying ages. There appear to be two important factors influencing this response which we had to investigate, namely: (1) The circulating passive antitoxin present at the time of the first injection, and (2) the age of the baby at this time.

In order to gain some information about the circulating antitoxin we Schick-tested 71 expectant mothers at the 4th month of pregnancy, and immunized those who were Schick-positive with 2 doses of A.P.T. at an interval of two months. Bleedings were then taken from all the mothers a few weeks before delivery. Antitoxin estimations were performed by Mr. Glenny and Miss Barr on these specimens, on cord blood samples, and on blood

samples taken from the infants at intervals of about two months. The children were bled by heel-prick using a special scoop designed by Mr. F. Tottem, which is detachable from the 3 by  $\frac{3}{8}$ " tube on which it is used, and is easily sterilized by boiling. The tubes contain potassium oxalate in solution, and the antitoxin in the plasma is estimated. We have, so far, taken over 190 bleedings from infants in the course of this investigation.

Mr. Glenny will give details of the gradual loss of passive antitoxin from the blood of these infants. The great majority had less than 0.005 unit (i.e. were below the Schick level) by the time they were 6 months of age. However, when there were high initial levels in the cord blood, some of the children retained their immunity for far longer periods. For example, in one case, with 120 units per ml. in the cord blood 0.2 unit was still present when the child was 11½ months old.

As the result of this series of estimations, we have available a chart from which the passive antitoxin present at any age up to 1 year can be calculated if the level in the cord blood is known.

We then immunized a number of babies of varying ages and with different amounts of passive antitoxin at the time of the first injection, in order to study the importance of these two factors.

The results so far investigated show that:

First, with regard to age, infants immunized in the 2-4 months age-group have responded as well as those over 6 months. Incidentally, 3 of the children were exactly 8 weeks old at the time of their first injection.

Secondly, with reference to the influence of passive antitoxin on the response, all except 2 of those shown on the main chart had less than 0.05 unit and the responses were generally good. Of the 3 children who possessed 0.05 unit one responded very well producing 1 unit six weeks later, and the other two produced 0.1 and 0.01 unit respectively.

Three infants with 0.1 unit and one with 0.2 unit all failed to respond.

We have also given 6 children their first injection at birth. One of these infants who had 0.04 unit before injection showed a slight response. Unfortunately, 4 of the remainder had 0.1, 0.2, 0.5, and 0.5 unit respectively in the cord blood specimens, and as expected, there was no antitoxin response. The sixth child in this group had less than 0.01 unit in the cord sample, and despite two injections of A.P.T. at birth and at 2 months, no detectable antitoxin was found in later bleedings. As the mother of this child was herself immunized during pregnancy and failed to respond, this suggests another factor which may influence the immunity response, namely, an inherited inability of the infant to produce certain antibodies.

These results suggest two very important conclusions:

(1) That infants of 2 months and probably less, injected with A.P.T., will produce diphtheria antitoxin as well as those over 6 months.

(2) That a reasonable response may be expected provided there is not more than 0.05 unit of passive antitoxin present at the time of the first injection with 0.5 ml. A.P.T.

The number of infants so far investigated is small but in view of the results already obtained we are now immunizing a large number of babies during the first 3 months of life. I would like to say that the injection of babies under 4 months is far less upsetting to the child, and a more rapid procedure than when it is performed at the age of 9 months or later.

In order to get some idea of the immunity of the population at the present day, we have tested two random sets of 100 cord samples from Guy's and St. Alfege's Hospitals respectively. Although, in the main, these results are comparable, there were 5% more below Schick level in the St. Alfege's series. This difference in two similar social districts is interesting, but probably of no importance if examined statistically. These figures show that the percentage of non-immune females in these two districts is between 25 and 30% at the present day.

One further interesting feature has been revealed by the testing of these cord samples: if the 50 samples from the original mothers who were Schick-tested and found to be negative are compared with 50 controls (not Schick-tested) from the same district but with serum antitoxic values above the Schick level, the lowest recorded value in those who were Schick-tested was 0.04 unit with an average for the 50 women of 0.776 unit. The average for the controls with 0.01 unit or more was 0.203 unit. Thus, treating the two populations as immunologically similar, 50 Schick-negative women gained an average of at least 0.5 unit over those women not injected with the Schick dose of toxin. In actual fact, the gain must have been even greater as the Schick test in most cases was performed at least four months before delivery; with the lapse of time the antitoxic level may have passed its peak. Also, 23 of those who were Schick-tested had cord bloods of 1 unit or more, whereas only 4 in the control group reached these values. Mr. Glenny will discuss the significance of these findings.

The secretion of diphtheria antitoxin in colostrum and milk has also been investigated

in a number of cases. The antitoxin content in the milk falls very rapidly during the first three to four days reaching a basal level within a week. Comparison with the volume of milk secreted which continues to increase gradually for nearly three weeks shows that the decrease of antitoxin content is not due solely to dilution but probably also to the rapid decrease in the globulin content of the milk in the first few days after delivery.

In the near future, we intend to see if the relatively high colostrum levels are of any significance in prolonging the passive immunity of the infant: non-immune newborn infants will be fed with colostrum collected from high-titre mothers. This will be followed by testing blood samples from these babies to see if any absorption of antitoxin has occurred.

*Summary.*—Natural antitoxic immunity in the population investigated appears low at the present day. Consequently, a large number of newborn infants (25–30%) lack antibodies against diphtheria.

Our results show that active immunization of infants is practicable at 2 months, and probably earlier, provided that there is not more than 0.05 unit passive antitoxin present at the time of the first injection.

*Acknowledgments.*—I should like to express my appreciation of the co-operation that I am receiving from the Staffs of the Maternity Departments of St. Alfege's and Guy's Hospitals, and particularly to Miss L. Coombe, Superintendent Health Visitor at Salomon's Welfare Centre, without whose assistance this investigation could never have been undertaken.

#### Mr. A. T. Glenny:

The work on lambs described by Miss Barr and that on babies by Dr. Randall has shown that it is not impossible to immunize the very young, provided that the level of maternally conferred passive antitoxin is not too high to cause interference. Babies lose their passively acquired immunity to diphtheria at the rate of 20% during each week of the amount of antitoxin present at the start of that week; after about 10 weeks the rate of loss decreases to about 15% per week. From their results it has been possible to determine the age at which any baby with a known amount of antitoxin in the cord blood reaches a sufficiently low concentration to permit of active immunization and also that at which without immunization the child would become susceptible. The first of these two levels to be reached can be taken as 0.05 unit per ml. if the first injection is to consist of 0.5 ml. A.P.T. or 0.02 unit if 0.2 ml. is given. Incidentally it was pointed out that it is more logical to give the larger injection first. The amount of antitoxin that is too low for adequate protection can be taken arbitrarily as 0.004 unit per ml.

Two schemes of immunization are possible: one, involving a somewhat elaborate organization, is to test every cord blood and fix a suitable age at which each individual child should be immunized; the other consists of testing a representative sample of 100 cord bloods and calculating the age at which the great majority of children can be safely immunized. Applying this method to the information at present available it is recommended that the first prophylactic injection be given to each child when 3 to 4 months old. If immunization is delayed until the last few children will respond fully to immunization, over 90% may be exposed to the danger of infection for several months longer than necessary. Some 20 to 30% of the population have insufficient antitoxin at birth or lose what they have within a few weeks. Should there ever be need to immunize such children as quickly as possible they can be detected by a Schick test upon all mothers a few days after delivery. Injection with Schick toxin beforehand so increases the mother's antitoxin and the distribution of cord blood values is so altered that the age at which some of the children can be successfully immunized may be delayed for some months and others might remain unchanged. Schick-testing during pregnancy is not the only factor influencing the distribution of cord blood values. Few of the mothers of to-day have been actively immunized but soon the proportion will increase rapidly due to the effect of mass immunization started eight or nine years ago. It is difficult to predict the relative extents to which this will increase the passive immunity of the young compared with the decrease due to the lower incidence of diphtheria reducing the opportunities of natural immunization. There is a real need for periodic surveys of the immunity-status of the general population by means of antitoxin tests on a number of cord bloods. The most suitable scheme for immunization to-day may be quite unsuitable within a few years.

The advantage of early immunization is not limited to saving the lives of the few babies who otherwise might die of diphtheria, while still less than 1 year old. The earlier the first injection, the greater the dose which can be injected and the longer the interval which can be left before the second injection. Both these factors contribute greatly to the establishment of good basal immunity and may lessen the need for subsequent boosting doses.

Large-scale investigations into a number of problems should be officially put into operation so that diphtheria immunization may be established on a more scientific basis.

## Section of the History of Medicine

President—E. ASHWORTH UNDERWOOD, M.A., M.D., D.P.H.

[November 3, 1948]

### Antonio de Gimbernat, 1734–1816

By N. M. MATHESON, F.R.C.S.

It is not easy to ascertain why the life of Antonio de Gimbernat has been so neglected in our medical biographies. Living under the shadow of Haller has detracted from an appreciation of many a man, but it scarcely explains the silence on Gimbernat. No single article dealing with his career have I seen from British or American sources. Yet, even to-day, the name of Gimbernat is known to every medical student; this is not from the literature, but simply because his ligament, like Hunter's femoral canal, has proved particularly resistant to changing anatomical nomenclatures.

Was not Gimbernat Scarpa's rival? He saw at close range the activities of three successive kings. Could not Gimbernat claim the position of first surgeon of his day in Spain? He completely revived Spanish medical education. It was Gimbernat who, advising on the claims of Jenner, was instrumental in sending F. Xavier Balmis on the amazing voyages of the *Maria Pita* and the *Magellanes*.

On the shore of the Mediterranean to the south-west of Barcelona lies the Catalan province of Tarragona. Arnold of Villanova knew it well and so did Ramon Lull. On the Tarragonian coast was the Roman town of Oleaster, rebuilt by Alberto Cambrils, whose name it bears to the present day. It was in Cambrils that Gimbernat was born in 1734.

By his own initiative, and with some local help, Antonio de Gimbernat was able to learn Latin at Riudoms and to take an arts course at Cervera—a small town to which Philip V had transferred the University from Lleida.



Portrait of Gimbernat.

(With acknowledgments to the Enciclopedia Universal Ilustrada Europeo-Americana (Barcelona)—1907.)

It had been the lot of Catalan medicine, shortly before Antonio de Gimbernat was born, to have the Universities of Barcelona and of Lleida disbanded, as a punishment for the fight of the Catalans on the side of the English, Dutch and Austrians against France and Spain in the War of the Spanish Succession. A University was created by Philip V in the small town of Cervera to replace the suppressed Universities, and it seems to have been the



purposes of the King and his advisers, in creating a new University in a small and distant place, to bring the already declining creative intellectual capacity of the Catalans finally to its end. But, paradoxically, it was from Cervera that Gimbernat emerged, and with him the revival of the Catalan school of surgery took place. His teacher, Pere or Pedro Virgili (1699-1776), also from Catalonia, had studied medicine in the University of Montpellier, which, until it had been absorbed by France, had been the most important cultural centre of Catalonia and of the whole area of South France that spoke Langue d'Oc. In the absence of a medical school in Catalonia, Montpellier was the place where Virgili went to learn anatomy and surgery, as Arnold of Villanova and Ramon Lull had gone five centuries before him. As modern surgical teaching was then impossible in Catalonia, he obtained the royal consent to establish, in 1748, a Royal College of Surgery in Cadiz, where as a Surgeon-in-Chief to the Spanish Fleet he held a position of great authority. This was principally a Naval Medical School and there it was that Virgili met Gimbernat, following a pre-clinical course remarkably similar to that of to-day. Physics, chemistry and botany were in the curriculum with, of course, anatomy and physiology. Medicine followed the lines of Van Swieten. Virgili himself taught surgery. Judging from his medical knowledge and operative courage one can assume that Gimbernat's studies were supervised by an exceptional man. In most subjects Gimbernat excelled. Dissection occupied much of his leisure. While still a student he made original observations on the peritoneal folds and on congenital anomalies.

After the college of Cadiz had proved its worth, Virgili used his personal influence on the grandson of Philip V, King Carlos III, to obtain permission to establish a Royal College of Surgery in Barcelona, which he succeeded in procuring in 1760. Two years later Antonio de Gimbernat was appointed Professor of Anatomy there and began the teaching of surgery which initiated the modern surgical school of Barcelona.

Gimbernat was still under 30 when he undertook the responsibilities of his first Chair—the Professorship of Anatomy at the Royal College in Barcelona. He was also a practising surgeon. Gimbernat soon married. He was to have six children; three sons we hear of later. *Carlos*, the lithographer and a medical man of vast learning in literature and science. *Antonio*, the agriculturalist, and *Augustin*, His Majesty's Consul in France and the author of a short biography of his father.

In Barcelona, Gimbernat accurately described the reflexion of the inguinal ligament. There he set about those researches and performed those operations which prepared the way for a book—*Nuevo método de operar en la hernia crural*. This he was in no great hurry to publish. Not until 1793 did that work appear. An English edition soon followed, translated by none other than Thomas Beddoes. Later came French and German translations. Little known in England is the Spanish edition which was printed in Granada as late as 1916 on the occasion of the centenary of Gimbernat's death.

It was during those very early Barcelona years that Gimbernat began directing attention to diseases of the eye; with ophthalmology his name was to become particularly associated.

At this time Carlos III was engaged on real practical progress. In 1774, at the express wish of the King, Gimbernat was selected to report on the conditions of hospitals abroad.

His companion was Mariano Ribas. In Paris they attended the Clinics of Louis and Desault. By the year 1777 Gimbernat was already in England.

I am indebted to Dr. J. Trueta for bringing to light a fact which has, so far, been overlooked by scholars and medical historians alike. The Catalan scholar Bishop Felix Torres-Amat, in his *Diccionario Crítico de los Escritores Catalanes* (Barcelona, 1836, p. 287), points out that:

"In London he (Gimbernat) attended the lectures of Hunter (John) and of Saunders. Voluminous MSS. have been preserved in which he himself wrote all these lectures, the majority of them in English; 93 belong to the course of anatomy by Dr. Hunter and among them several practical cases and clinical observations are described, together with several demonstrations of injections of the blood vessels. In lecture 8 the above-mentioned Dr. (Hunter) spoke of hernia and of the operations for its cure. After the lecture Sr. de Gimbernat addressed Dr. Hunter publicly and described the method he had invented to operate upon femoral herniæ with complete security. The latter listened attentively to the details of this interesting invention of Sr. de Gimbernat and, convinced of its greater security, gave his approval and promised he would practise this method thereafter. . . . He (Gimbernat) wrote in London in 1776 a MS., which he entitled *Practical Notes*, relating to surgical operations performed at St. Thomas's Hospital, Guy's Hospital and St. Bartholomew's Hospital."

Where is this most valuable MS. and where are the other MSS.? No one seems to have seen them since the time of Torres-Amat, who had been in personal contact with Augustin, the son and biographer of the great surgeon. Torres-Amat tells us in a short biographical

note he wrote on Augustin de Gimbernat that: "The love of his country moved him to place a bust of his brother Carlos (the naturalist), and all the MSS. in his possession, at the disposal of the Catalan Library." It is not unlikely that the Gimbernat MSS. are buried among the unclassified papers in the Library of the University of Barcelona, or among those of the Library of Catalonia (Biblioteca de Catalunya).

From England, Gimbernat and Ribas went to Scotland to observe the methods of Cullen before proceeding to Holland where Pieter Camper was a great attraction.

Returning home Gimbernat resumed work in Barcelona, but not for long. In 1779 he and Ribas were called to Madrid to draw up plans for a new Medical School. A certain amount of opposition had to be overcome. It was not until eight years later that Gimbernat delivered the Inaugural Address at the Royal College of Surgery of San Carlos. His subject is not without interest—*On the Correct Use and the Mis-use of Sutures*—never an easy theme upon which to speak.

Yet another task allotted to Gimbernat was the establishment of an anatomical and pathological museum. Luis Comenge [1] tells us that within six years the Madrid Museum had no rival in Europe and those who have examined Gimbernat's specimens can well believe it. Botany was included, as might be expected from one who knew Holland, hard on the heels of Boerhaave and Linnaeus. At the college of San Carlos, Gimbernat most efficiently combined the office of Co-Director with the Professorship of Operative Surgery.

In Madrid he spent some most arduous years. I can make only a brief reference to some of the achievements of that long and varied career, which ended when Gimbernat died at the age of 82 years—sadly afflicted with bilateral cataract, a disease on which he was an unquestioned authority. His life was not without its interruptions and adventures; when we consider the background of his boyhood we recall that the British were in Barcelona at the beginning of Gimbernat's century. As a man, he had the confidence of very different kings. In his old age, Napoleon was after Madrid and Gimbernat was present on May 2, 1808, when the inhabitants rose in a body against Murat and the French garrison.

Gimbernat wrote much on the diseases of the eye, on corneal ulcer and cataract in particular. His *Disertación sobre Las Ulceras de los Ojos* described the clinical features, differential diagnosis, and treatment of corneal ulcers as they had not been dealt with before. It was read before the Society of Medicine of Paris in 1800. For years *Gimbernat's Collyrium* had its place in the pharmacopeia. In London before the war one could judge his worth. In the Museum of the Royal College of Surgeons in Lincoln's Inn Fields were two cases of models illustrating in detail the pathology of the eye. Those exhibits, made under Gimbernat's supervision by Josef Valls, were of a perfection seldom seen at the present day. The numerous preparations, described in a letter from Gimbernat to William Clift, bore striking testimony to the high standard of ophthalmology in Gimbernat's hands. It is fortunate that we have kept a list of those demonstrations, for the specimens were lost for ever during the bombing on the night of May 10, 1941.

Gimbernat was a surgeon in the true sense; his practice was of the widest, as was the custom with the great doctors of his day. Already we have referred to the work on strangulated femoral herniæ. Plates from his book show that Gimbernat knew how to demonstrate his ligament, not from below, but from above. The beautiful illustrations, in sagittal section, make one wonder why, with the advent of anaesthesia, a mid-line approach was not advocated until A. K. Henry described his particular operation.

When first the name "Gimbernat's ligament" came into general use in France and Spain I do not know. In London, John Hunter certainly acknowledged Gimbernat's priority in 1777—nearly ten years after the Barcelona description. William Hey of Leeds, whose long life so closely corresponds to that of Gimbernat, was quick to use the term. Hey described a ligament in the groin which bears his name. Sir Hugh Lett [7] tells us that Hey himself in order, as he said, to avoid a disagreeable periphrasis named Gimbernat's ligament after the surgeon to the King of Spain, Don Antonio de Gimbernat, who first described it.

Gimbernat was a good surgical anatomist and some of his own surgical instruments showed great ingenuity. There were special ones for cataract operations, others for removing urinary calculi, and one for operating on the ear. Gimbernat had his own technique for the radical cure of hydrocele. We should note that he advocated and practised gradual compression of the main arterial trunk in the treatment of aneurysms.

If we are to use eponyms in medicine, it seems that the term "Cloquet's Gland" properly belongs to Gimbernat. Of the natural sciences I am in no position to speak but Gimbernat wrote, briefly it is true, on his three months' observations in the geology of the Alps. In botany and botanical gardens he was always interested and there is a plant known as the *Gimbernatia*.

Towards the close of the eighteenth century concern was growing over the death roll from smallpox in the Spanish possessions overseas. A great scientific expedition was

organized to carry the benefits of vaccination to the New World. It was to proceed not only to Mexico, but also along the Venezuelan coast, over the Andes, and across those vast stretches which led to the Spanish settlements on the Rio Plata. In 1803 Francisco X. Balmis, a surgeon from Alicante, set off on that amazing voyage. Preservation of the virus was a problem, overcome in a practical manner. Sailing with the ships were 22 boys; at the outset one was inoculated. From arm to arm, from boy to boy, the virus was carried to the Indies.

At Caracas, the expedition subdivided. The leader of the party which traversed the South American continent was Dr. Salvany, a graduate from the College of Surgery in Barcelona. From Venezuela, Balmis made his way to Havana, sent a detachment to Guatemala, and led his men to Mexico. But that was not all; on went Balmis, with another 26 boys, to the Philippines, Canton, around to Lisbon and back to Madrid. But why these diversions from surgery to public health? Dr. S. F. Cook [2] informs us that seldom, perhaps never, in the history of medicine has there embarked an expedition so grandly conceived, so well executed, and so uniformly successful. Its preparation left nothing to be desired and the chairman of the first Scientific Advisory Committee was Antonio de Gimbernat. Having studied surgery at St. George's under Mr. Hunter, Gimbernat surely kept an eye on the activities of Dr. Jenner.

To select Gimbernat's main contribution presents difficulties; he had so many interests. Perhaps it was as an organizer, as a dean. For years Gimbernat advised with outstanding wisdom on all kinds of surgical and medical matters. Quite late in life he was occupied on the planning of yet another contemplated medical school at Pamplona, which was to benefit from the experience of the Barcelona and San Carlos successes.

Gimbernat had responsibilities at Court and responsibilities at the Universities and hospitals, but the anatomy commenced at Cadiz remained as a relentless study, in an alert and observant way. Surrounded by increasing administrative activities, Gimbernat continued to train surgeons and to justify his favourite and oft-quoted remark, "mi autor más favorito es el cadaver humano".

As a co-ordinator of medical practice Gimbernat will be remembered. "Medicine for the surgeons and surgery for the physicians" were his actual words. Gimbernat's interest in vaccination showed that he meant what he taught.

These are but some of the contributions of one of the masters of Medicine in Spain. As the founder of Schools of Anatomy his place is secure. Since, however, this great Catalan—pioneer in ophthalmology, vascular surgery and urology—has more than once been described as a herniologist, we must add that it was at a time when that peculiar term put one in good company; it had been applied to Antonio Scarpa, to Astley Cooper, and even to Pieter Camper.

#### BIBLIOGRAPHY

- 1 COMENGE Y FERRER, LUIS (1914) *La Medicina en el Siglo XIX* Barcelona, 249.
- 2 COOK, S. F. (1942) *Bull. Med.*, 11, 543; *Bull. Med.*, 12, 70.
- 3 FERNANDEZ, V., and SERRET ZULOAGA, J. (1932-33) *Trab. cated. hist. crit. Madrid*, 1, 233-260.
- 4 GARCIA DEL REAL, E. (1921) *Historia de la Medicina en Espana*, Madrid.
- 5 — (1922) Addendum to Spanish translation of F. H. Garrison's *Introduction to the History of Medicine*, Madrid, 463.
- 6 HERNANDEZ, MOREJÓN A. (1842-50) *Historia Bibliografica de la Medicina Espanola*, Madrid, 6, 285.
- 7 LETT, SIR HUGH (1942) *Univ. Leeds Med. Soc. Mag.*, 12, 94.
- 8 "M." (1917) *Chron. Med.*, 24, 119.
- 9 MATHESON, N. M. (1945) *Brit. med. Bull.*, 3, 238.
- 10 TRUETA, J. (1949) Personal Communication.

[January 5, 1949]

## **Eighteenth Century Medical Care: A Study of Roxburghshire**

By IAN E. McCracken, M.D., B.Hy., D.P.H.

IN some respects the medical history of the eighteenth century is almost too rich—rich to the point of deception, for it has been written up so fully and well in certain directions that it is all too easy to lose sight of its deficiencies.

One of its lacunæ is its failure to give any clue to the real availability of medical care in the period, or, to put it plainly, to show how the common people received medical advice and treatment. Relatively speaking our knowledge of the way the art of medicine reacted to the more scientific and liberal outlook that dates from about the mid-century leaves little to be desired. The effects of that intellectual renaissance on the practice of medicine have been closely studied. Innumerable examples spring to mind—Lind's code of hygiene for the Navy, Pringle's specialized Army Medicine, Hunter's contributions to surgery, and

Smellie's to midwifery, a new school of clinical teaching in Edinburgh under Cullen and Andrew Duncan the Elder, the establishment of hospitals and dispensaries and the spread of preventive medicine practices generally.

All this contrasts strangely with the slenderness of our information about domiciliary medicine in the same period. While historical research has floodlighted the great advances in medicine we would still be hard put to it to show clearly whether the majority of the subjects of George III, urban and rural, sought or received medical advice as freely as those of either Anne or the young Victoria.

It may be said the very fact that in the course of the century some dozens of general hospitals were founded in London and the main provincial centres and that they were quickly followed by the establishment of dispensaries and special hospitals such as fever hospitals is a good measure of the growth of a healthy contemporary interest in medical care. It may be felt that the records of these institutions, where they have survived, contain all the information we need for a reasonable reconstruction of the medical care position; and it is perfectly true that hospital and dispensary records do reveal a good deal about *town* medicine. But unfortunately these institutional records being related, with very rare exceptions, to urban conditions and urban populations, throw very little light on what was going on in rural and semi-rural areas where the great bulk of the population lived—as much as 80% of it even at the end of the century according to Weber [1]. So that eighteenth century town medicine is scarcely more representative of the position in the country as a whole than rural medicine would be to-day. That being so, is there any way of getting closer to the social relations and economic significance of medicine in the rural, and consequently the more typical, England or Scotland of the eighteenth century? The answer depends on whether the surviving local records for small market towns, villages and hamlets contain the kind of information we need.

It would be ridiculous to expect any great wealth of relevant information from these sources, but there are two questions which are fundamental in relation to the medical care of any community at any date and if local records from appreciable areas in different parts of the country could provide answers, or even partial answers, to these questions the net result might be illuminating. The questions are these: What was the proportion of doctors to the population? and, How were they distributed? This paper is primarily the record of an attempt to find answers to these questions for one "appreciable area" during the latter half of the eighteenth century; it tests from the medical standpoint, so to speak, the utility of local records and other contemporary sources in one fair-sized rural county. It was as a matter of personal convenience that the county selected for the experiment was the Scottish county of Roxburghshire.

#### ROXBURGHSHIRE

This county occupies almost 1,000 square miles of the south of Scotland. Throughout the eighteenth century its economy was based entirely on agriculture and despite marked differences in the quality of land that ranged from the heights of the Cheviots to the fine valley of the Tweed no district benefited more from the "improved agriculture" of the period; so that though it comprised no more than 3% of Scotland's total area it accounted for at least 10% of her "valued rent" [2].

As well as becoming a prosperous county it was always a beautiful one.

'Tis Beauty all and grateful song around  
 Joined to the low of kine and numerous bleat  
 Of flocks thick nibbling thro' the clovered vale.

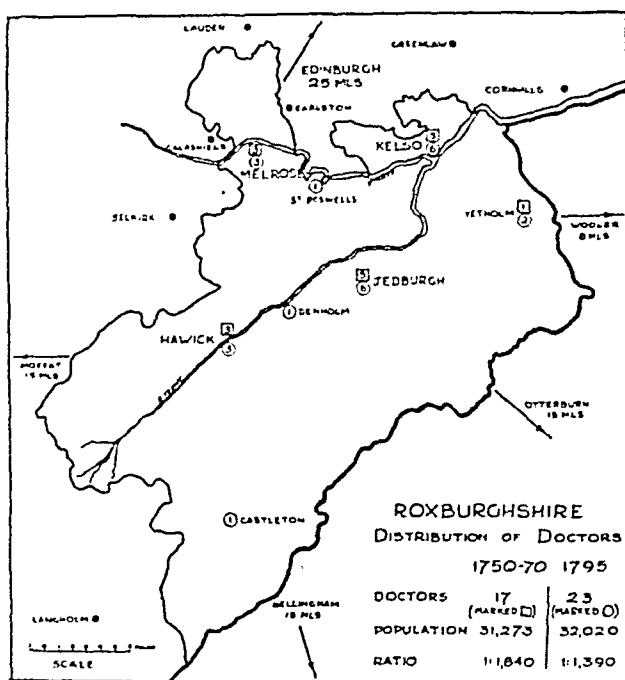
So wrote James Thomson, the county's native poet, in 1730. And if, presently, it seems that the county attracted a disproportionate number of doctors to settle there the inducements of a district both prosperous and pleasant must be borne in mind.

Prior to about 1770 movement through the county was hampered by lack of decent roads and bridges. But after that date mobility was improved by the opening of four good stretches of turnpike road and by an increase in the number of bridges over the Tweed and the Teviot to two in each case [3]. It will be shown that these changes, which must have meant a good deal to the doctors, do correspond in time with a definite alteration in the scatter of doctors over the county.

As to population, there are fortunately two reputable eighteenth century estimates of Scotland's population by counties—Webster's in 1755 [4] and Sinclair's in 1795 [5]. According to these, Roxburghshire's population remained very stable over half a century; Sinclair's figure of 32,020, or about 2% of the whole country, being only 747 more than Webster's early estimate.

The county contained no large town during the century and though the nearest was about 45 miles, or a good day's ride, from the centre of the county, it was Edinburgh—Edinburgh in the heyday of its glory as a medical centre and not without its influence on medical care

even at this distance. Of its own four small towns Kelso, the largest, had a population of 4,324, Jedburgh, 3,288, Hawick, 2,928 and Melrose 2,446 [5]. The landward part of the county was divided into 31 parishes. Generalizing with the aid of Sinclair's Statistical Account of Scotland, a typical lowland parish consisted of a principal village of some 200-300 inhabitants, fifteen to twenty farm hamlets with 30 to 40 inhabitants in each, the mansions of three or four resident landowners and a variable number of isolated small farms and cottages, giving the parish a total population of rather under 1,000. In the hill



parishes there was hardly anything that could be called a village and the number of hamlets and small farms was rather greater.

From all this description Roxburghshire emerges as an ideally uncomplicated setting for the study of eighteenth century rural medicine.

In the period under review local government, such as it was, was mainly carried out for each parish separately by the Kirk Session—a body that corresponded roughly to the Vestry of an eighteenth century parish in rural England. One of the principal responsibilities of the Kirk Session was to provide for the parish poor and in consequence the Session was involved to some extent in questions of medical relief. Medical relief at times meant the services of a doctor and it is these Sessions' records, their minutes and accounts (too lightly regarded storehouses of social history but in the main miraculously preserved) that form one of the key sources of information about local doctors in Scotland. Emmison [6] in a study of a Bedfordshire parish has already noted that the comparable material, the minutes of the Vestries and the accounts of the overseers of the poor, contains the best surviving and untapped sources of information about doctors in eighteenth-century England.

#### THE NUMBER OF DOCTORS AND THEIR DISTRIBUTION

The map shows the number of doctors residing and practising in Roxburghshire, and the way they were distributed over the county at two different periods, in 1750-70 and again in 1795.

It will be appreciated that the nature of the source that will yield evidence of the existence of doctors may differ not only from place to place, but from time to time in the same place. When Kirk Session records fail for any reason the clue may come, for example, from a local newspaper, a biography, Masonic Lodge records or from the records of some other local society or institution. Even so there are places where the trail can only be picked up spasmodically over the years and it is generally impossible to pin down the number of doctors for all places to *precisely* the same year.

It is for this reason that the earlier phase covered by the map has had to be quoted as

referring to a twenty-year span, 1750-70. In the case of the 1795 phase the difficulty is minimized by that social history windfall, Sinclair's Statistical Account of Scotland. Published in 21 volumes between 1791 and 1798 it makes the evidence so much clearer for those years that it can be brought to a focus at what may be called "*circa* 1795"; and since "*circa* 1795", when there is evidence of the presence of 23 doctors in the county, is the better founded of the two phases it will be simpler to consider it first.

Sinclair's Account has something to say about every parish in Scotland; a separate report was made on each, as a rule, by the minister of the parish. The reports on the different parishes vary enormously in size and in value. Some of them mention the health of the parish and its prevalent diseases, and about one in ten has a word to say about the presence or absence of doctors in the parish. Fortunately, in the accounts of four of the Roxburghshire parishes—Kelso, Jedburgh, Castleton and Yetholm—we are told about the doctors.

Take Jedburgh—the minister in his account to Sinclair states that there are "three physicians and three surgeons" in the parish [7]. The minister of Castleton mentions that there is "a surgeon in the parish" [8]. The Yetholm minister says there are "two doctors in the parish" and adds "one of them has given over business" [9]. For some reason it was not the parish minister but Dr. Christopher Douglas, the leading physician of the town, who wrote the Kelso account for Sinclair. He gives a list of occupations and includes "medical practitioners—6" [10]. It was a typically gracious gesture on the part of Dr. Douglas to use a phrase that included the inferior surgeons and apothecaries in the same category as himself.

On the face of it there is no reason to doubt the accuracy of these statements: but they can be checked, and mentioning how this can be done will show what sources of information about eighteenth century rural medical practice can still be found.

In the case of Kelso checking is particularly easy, for in 1795 there had been a public dispensary in the town for nearly twenty years; its records have all survived and in them are several indications of the number of doctors practising there [11]. Confirmation of Castleton's one doctor comes from a letter written to the local newspaper, the *Kelso Mail*, in 1798; the writer refers to inoculations against smallpox being carried out "by the surgeon who resides in the parish" [12]. It is the *Kelso Mail* that confirms the presence of two doctors at Yetholm, shows it was a father and son partnership and even reveals what lay behind the Minister's remark that one of the doctors there "had given over business", for three years later the paper announced [13] that, though Dr. Walker "who had been so long in practice at Yetholm had died there at the age of 83", his son would continue to practise there. Checking the presence of three physicians and three surgeons in Jedburgh is a more complicated business. Three of them can be traced through Kirk Session records (using the records in a way that will be described in detail in relation to St. Boswells), one through an obituary notice in the *Kelso Mail* [14], another through a reference in Robert Burns' diary [15] to his hospitality to the poet during a journey through Roxburghshire and the last through the autobiography of the same minister who wrote the Jedburgh account for Sinclair [16].

Sinclair's Account, alas, gives no further help and doctors in any of the remaining parishes have to be tracked down by other means.

St. Boswells offers a good example of the way in which this aspect of the medical history of even a small village can be pieced together from its Kirk Session records. On going through the St. Boswells Session disbursement accounts for the last decade of the century it is found that occasional small payments have been made to Dr. John Mein. In these records, as in all session records, references to medical relief are scant, but one such reads: "August 13th, 1796. To Dr. John Mein for attending Mary Muir per receipt £1 0s. 0d." [17]. The records show that Mary Muir is an old parish pensioner who has been receiving 5s. a month for some years, but, unfortunately, they tell us nothing about the nature of her illness or what attendance Dr. John Mein gave for his £1. That Dr. Mein lived at St. Boswells is confirmed by the parish baptismal roll where the names of his children are registered. No other doctor is referred to in the parish records during Dr. Mein's time: but it is needless to speculate about the possibility of there being a second doctor at St. Boswells for it is surprising enough to find one man making a living there when the population of the whole parish was only 500 and when there were doctors in the neighbouring parishes of Melrose and Earlston in Berwickshire.

The poorness of the practice at St. Boswells is dramatically confirmed on examining the Session's accounts for subsequent years. They reveal the experience of the doctor who succeeded Dr. Mein in about 1803, a Dr. Oliver, to whose skill a local biography, bears testimony [18]. Yet after twenty years there Dr. Oliver himself became a pensioner of the parish, receiving regularly from the Kirk Session his coals, firewood and meal and, occasionally, gifts such as a few shillings in cash, a pair of shoes, a hat or a great coat (noted as costing 19s., and 6d. for carriage). Though there is evidence that forty years earlier one of the

Hawick doctors reached a similar degree of destitution [16], poverty was not the typical experience of a Roxburghshire practitioner of the period. On the contrary, when the matter can be tested, they seem to have prospered, for at least four retired to comfortable little estates in the county, "another became a considerable property owner in Kelso and there are several examples in the half-century of sons succeeding happily to their fathers' practices.

Denholm, where the map shows one doctor, has no eighteenth century session records of its own for it was not then a parish. But after 1775 the neighbouring parish of Minto, which up till then had occasionally employed a surgeon from the much more distant town of Jedburgh, began to use the services of Mr. Turnbull "surgeon in Denholm" [17] and that is also his address in the list of the Hawick Subscription Library in 1790.

In the case of Hawick it happens to be easier to find the local doctors from the town's valuation roll for the poor rate in 1789 [19]. The roll covered all the dwellings and followed the good old-fashioned custom of putting a man's occupation after his name. It shows one physician and two surgeons in the town with assessed rentals of £7 5s., £4 5s. and £3 respectively and since the highest assessment was £12 10s. and the lowest 10s. it furnishes a rough indication of the status of the doctors. The names of these three men are also to be found in the records of the neighbouring Kirk Sessions showing that they were all in active practice.

After every other known source of information has been tapped Melrose remains as the one parish not already mentioned in which there were practising doctors. There, as it happens, the records are poor and the important cash accounts of the Kirk Session have not survived, but those of the neighbouring parishes of Galashiels and Bowden [17] refer to a physician and a surgeon who were evidently practising in Melrose in this period. There is less satisfactory evidence of a second surgeon who appears to have practised in the town at the same time. He is named as a father, and is designated surgeon, in the baptismal roll for 1793 and again for 1794 and he lived right in the town, a thing he was most unlikely to have done had he been of independent means. Further it can be shown both for an earlier period and subsequently that Melrose was a three-doctor town, so that it seems proper to mark it on the map as such in 1795. With this single exception the evidence for every one of the 23 doctors of the date being in active practice is unequivocal; an important point in view of the number of retired doctors living in the district who must be rigidly excluded from any list that purports to show only practising doctors.

Given 23 as the number of doctors and 32,020 as the population of Roxburghshire it is still not permissible without considering one further point to say that 1 to 1,390 truly represents the district's doctor/population ratio in 1795. The county boundary meant nothing to the doctors. The real doctor/population position could be very different if Roxburghshire was a county that was a greater or lesser exporter or importer of medical services, so to speak, than the neighbouring counties. Fortunately something can be done to assess the significance of this factor.

Just as it is generally possible to show for Roxburghshire where each parish drew its medical services from, so with adjacent parishes in the neighbouring counties. When the position is examined in this way it is found, for example, that Kelso doctors penetrated deeply and regularly over the county border into both Berwickshire and Northumberland. While, on the other hand, it is found that doctors from a circle of places in neighbouring counties, from Lauder and Earlstoun in Berwickshire, from Selkirk and Galashiels in Selkirkshire and even from Langholm in Dumfriesshire at times rode over the boundary, but only into the fringes of marginal parishes in Roxburghshire. To the south where the Cheviot Hills and the barren moors of north Northumberland lie, the question did not arise. Certainly the overall impression is that Roxburghshire's medical service exports and imports were near a balance and that a ratio of one doctor to every 1,390 inhabitants in 1795 is a fair representation of the position.

To enumerate the practising doctors for 1750 to 1770, or roughly a generation earlier than the period just considered, is a more difficult and a less satisfactory task. There is nothing like Sinclair's Account or a county newspaper for this earlier period and the ravages of time have reduced the number and lessened the decipherability of the Kirk Session records. Some slight compensation, however, comes from two sources not so far mentioned. The one, containing innumerable references to local doctors and their work is the diary for 1755-61 of George Ridpath, minister of the Roxburghshire parish of Stichel [20], who, like so many parish ministers of his day, was well versed in medicine and treated by the doctors almost as a colleague. The other is a report on inoculation in Scotland prepared in 1765 by Alex. Monro, Sen. [21], which with its list of doctors practising inoculation, has value in confirming that certain doctors about whom there might otherwise be doubt were in active practice. Without entering into tedious and space-consuming details of the way the figures for this period, which add up to 17 doctors as against the 23 in 1795,

have been pieced together, it can only be said that from the evidence available they are the maximum numbers of doctors found practising in each place at any time between 1750 and 1770. If this figure of 17 be accepted for the doctors and Webster's estimate of the population in 1755 is used the doctor/population ratio at 1 : 1,840 is definitely less favourable than it was in 1795, as the following table shows:

MEDICAL PRACTITIONERS RESIDING AND PRACTISING IN ROXBURGHSHIRE

|                                              | <i>Circa</i><br>1750-1770         | <i>Circa</i><br>1795              | 1837                       | 1939                       |
|----------------------------------------------|-----------------------------------|-----------------------------------|----------------------------|----------------------------|
| Kelso .. .. .                                | 5                                 | 6                                 | 7                          | 4                          |
| Jedburgh .. .. .                             | 5                                 | 6                                 | 7                          | 3                          |
| Hawick .. .. .                               | 3                                 | 3                                 | 5                          | 6                          |
| Melrose .. .. .                              | 3                                 | 3                                 | 3                          | 2                          |
| Castleton .. .. .                            | 0                                 | 1                                 | 2                          | 1                          |
| Denholm .. .. .                              | 0                                 | 1                                 | 1                          | 1                          |
| St. Boswells .. .. .                         | 0                                 | 1                                 | 1                          | 2                          |
| Yetholm .. .. .                              | 1                                 | 2                                 | 2                          | 1                          |
| Total practitioners .. .. .                  | 17                                | 23                                | 28                         | 20                         |
| Population of Roxburghshire                  | 31,273<br>(Webster's<br>estimate) | 32,020<br>(Sinclair's<br>Account) | 43,663<br>(Census<br>1831) | 45,788<br>(Census<br>1931) |
| Ratio of practitioners to population .. .. . | 1 : 1,840                         | 1 : 1,390                         | 1 : 1,560                  | 1 : 2,290                  |

But whatever significance may be attached to the altered doctor/population ratio, surely the more important feature is the poorer scatter of doctors in the earlier period observable both in the table and in the map, for in rural medical practice it is on the scatter of doctors that the availability of medical services so largely depends. Three villages, it will be noted, Castleton, Denholm and St. Boswells, each of which had a doctor in 1795, had none in the earlier period. Nor is the evidence of this merely negative, for the relevant Kirk Session records<sup>1</sup> show that prior to 1790, 1773 and 1780 respectively these three parishes when arranging medical relief for a parish pensioner had to call on a doctor from a distance whereas after those dates the doctor in the parish itself was used.

What led to doctors setting up practice in these parishes can only be surmised. The reason would have been plain enough had there been significant increases in the populations of these parishes, but there were not [3]. In Castleton there was an actual decrease: but it was a hill parish without anything that could be called even a village in it until 1793 when the Duke of Buccleugh planned and built one [22], and it seems probable that it was the talk of a village that attracted a man there sightly in advance of its foundation. In the case of Denholm and of St. Boswells the likely factor is that following a Turnpike Act of 1768 [3] both became well sited from a doctor's point of view on new and important roads. Setting aside the cause, an interesting effect which can be observed from the table is that the scatter pattern for Roxburghshire's doctors that was adopted in the late eighteenth century became fixed in that form and has remained unchanged to this day. This century and a half old arrangement has been less affected by such changes in the doctor's *modus operandi* as the motor car and the telephone, than might have been expected, and it remains to be seen whether health centres or group practice will presently prove revolutionary enough to alter such a stable feature.

The table clearly invites comparisons between the doctor/population ratios in the eighteenth, nineteenth and twentieth centuries, but any that are made must be heavily qualified. No attempt, for instance, has been made to ascertain whether the position in 1837 was typical of the nineteenth century; 1837 figures have been given simply because Pigot's Commercial Directory of Scotland, which was published for that year only, provides a unique ready-made, and so far as it has been tested, reliable list of practising doctors for each county. Nor is it clear how far it is reasonable from the point of view of medical care to equate the work of a present-day rural general practitioner with that of an eighteenth century doctor who, in name at least, was either a physician, a surgeon or an apothecary and whose travelling time on his country round, taking 7 miles an hour as fair riding, was roughly four times greater than to-day. On classifying eighteenth century Roxburghshire's 23 doctors in an attempt to elucidate this point it is found that they comprised ten who were regularly styled "Dr." and called physicians, eleven who were always referred to as "Mr.—surgeon" and two who were sometimes referred to as surgeon and sometimes as "Apothecary—". Theoretically they should have restricted themselves to their traditional spheres: the physicians should not have taken apprentices nor performed inoculations nor

<sup>1</sup>The relevant records for Denholm are the Minto Kirk Session records.



treated such obviously surgical conditions as fractures nor done midwifery, but to quote only from Kelso's experience the physicians there did some or all of these things during the latter half of the century. One advertised for an apprentice [23], another inoculated [24], a third was paid by the Kirk Session of the near-by parish of Smailholm to treat a fracture [17] and a fourth continued to attend confinements some time after he had taken his M.D. degree and become styled physician [20], while the Kelso apothecary was also a competitor of the surgeons, at least in the matter of fractures [20]. It is true that one of the gentry would still have his physician's, his surgeon's and his apothecary's bills to meet at the end of the year [24], but on economic grounds exclusiveness in practice was obviously incompatible with rural conditions, and for the wider public the local doctor, whatever his strict professional status, was virtually a general practitioner: where there was a choice of doctor, as in the towns, it was the size of the patient's purse rather than the nature of his illness that determined which type of doctor he called in. Dr. Douglas was after all in tune with the times when, in writing an account of Kelso for Sinclair, he discarded the old terminology and grouped all the doctors under the single heading "medical practitioners".

Even so there are too many differences in the circumstances of the two periods to justify comparisons and it can only be said that it speaks well for eighteenth century Roxburghshire's attitude towards medical care that it supported such a surprising number of local doctors. And this surely is the crux of the business, this getting closer to the eighteenth century's attitude towards medical care: for the accumulation of figures showing the numbers of doctors one hundred and fifty years ago or information about their distribution can be of little or no value unless it leads to a better understanding of the contemporary outlook and ideas. In this respect this particular experiment has been gratifying. Its main purpose, and the one described in this paper, was to locate doctors. But in the process a good deal has been learnt about the wider aspects of medical care in this part of Scotland and as the task of following up some of these by-products of the investigation proceeds it is becoming possible to trace the evolution of a local policy of medical care that by the end of the century took practical shape in the establishment of two dispensaries, the one at Kelso and the other at Jedburgh, that were functionally different from the contemporary town dispensaries and well adapted to the special needs of this rural community.

Roxburghshire in this period, it must be borne in mind, was recognized to be politically and culturally progressive and until there is evidence from elsewhere it is wiser to assume that in its socio-medical developments it was also ahead of the times.

#### REFERENCES

- 1 WEBER, A. F. (1899) *The Growth of Cities in the Nineteenth Century*, 144. London.
- 2 SINCLAIR, Sir JOHN (1831) *Analysis of the Statistical Account of Scotland*. Edinburgh.
- 3 DOUGLAS, R. (1813) *A General View of the Agriculture of the Counties of Roxburgh and Selkirk*, Edinburgh.
- 4 WEBSTER, A. (1755) *An Account of the Number of People in Scotland*. Copy of MSS. (Nat. Lib. of Scotland.)
- 5 SINCLAIR, Sir JOHN (1798) *Statistical Account of Scotland*, 20, 621.
- 6 EMMISON, F. G. (1933) *The Bedfordshire Historical Record Society*, 15, 78.
- 7 SINCLAIR, Sir JOHN (1791) *Statistical Account of Scotland*, 1, 9.
- 8 — (1795) *Statistical Account of Scotland*, 16, 69.
- 9 — (1797) *Statistical Account of Scotland*, 19, 613.
- 10 — (1794) *Statistical Account of Scotland*, 10, 576.
- 11 MSS. Minutes of the Management Committee of the Kelso Dispensary, 1777, *et seq.*
- 12 *Kelso Mail* (1798) January 3.
- 13 — (1798) August 23.
- 14 — (1800) September 18.
- 15 CHAMBERS, R. (1851) *The Life and Work of Robert Burns*, 2, 81. Edinburgh.
- 16 SOMERVILLE, T. (1861) *My Own Life and Times*. Edinburgh.
- 17 MSS. Minutes and Accounts of Kirk Sessions. The Kirk Session records of Roxburghshire are retained by the minister of the parish to which they belong, except those of Lilliesleaf and Maxton prior to 1800 which are in the Church of Scotland Library.
- 18 YOUNGER, JOHN (1881) *Autobiography*, 256. Kelso.
- 19 *Hawick Archaeological Society Transactions* (1918), 13.
- 20 MSS. Diary of George Ridpath (Church of Scotland Library); also extensively published in the *Scottish History Society 3rd series* (1922), 2.
- 21 MONRO, ALEX (1765) *An Account of the Inoculation of Small Pox in Scotland*.
- 22 SCOTT, W. (1812) *Border Exploits*, 222. Carlisle.
- 23 *Kelso Mail* (1799) January 10.
- 24 MSS. (Privately owned) *The Household Accounts of a Roxburghshire Landowner from 1778 to 1809*.

## Section of Physical Medicine

President—L. C. HILL, M.D., F.R.C.P.

[January 12, 1949]

### DISCUSSION ON MANIPULATIVE TREATMENT

**Mr. J. Bastow:** Manipulations under anaesthesia, which are properly the prerogative of the profession, are dangerous unless in skilled hands, as the natural brakes of muscular resistance are removed and there is a tendency to do too much and so set up an excessive reaction.

There is a considerable scope in therapeutics for manipulation without anaesthesia, which should properly be performed in the Physiotherapy Department. This means that the Medical Officer in charge of the Department should possess the necessary knowledge and skill, both to carry out manipulative procedures himself and to impart this knowledge to physiotherapists under his direction.

*Essential preliminaries to manipulation.*—(1) A full diagnosis must be made in every case; manipulations should never be done without a preliminary diagnosis. (2) This entails at least two X-ray plates of the affected joint in every case. (3) An estimation of possible range by comparison with normal joint. (4) An estimation of the blood sedimentation rate and the plasma uric acid level are advisable in doubtful cases. An unsuspected case of tuberculosis or gout flares up very badly if manipulated and these conditions must be carefully ruled out. Urine tests should exclude diabetes. (5) Spinal manipulations under anaesthesia must be undertaken with caution, as cancerous metastases may be present and give rise to pain for weeks before X-ray changes are visible in the vertebrae. (6) In the case of the neck, spontaneous hyperaemic subluxation of the cervical vertebrae due to sepsis is not uncommon and must always be suspected if there is a history of recent infection.

*Cases suitable for manipulation, excluding major dislocations and fractures.*—(1) Joints, otherwise normal, where movement is restricted in one or more directions, owing to an adhesion. These cases usually follow minor trauma and respond exceedingly well to manipulation under anaesthesia. Post-operative adhesions come into this group. A full range of movement should be obtained and after-treatment should consist of frequent active exercises or games to ensure that this full range is maintained. Contrast hot and cold douching is helpful in relieving after-pain and in encouraging active movement by stimulating the local circulation.

(2) Where there has been a general restriction in the range of movement of a joint. This may be due to a variety of causes, often extra-articular, such as: (a) Prolonged neglect to put a joint through its full range; (b) fibrositis in the overlying muscles; (c) stiffness following prolonged splintage; (d) sepsis and subsequent fibrosis of extra-articular tissues; (e) hysterical fixation.

In such cases, manipulation must not be undertaken until the exciting cause has ceased to operate, i.e. local sepsis has subsided or need for splintage has passed. Because of the adaptive shortening of the extra-articular tissues, it is rarely advisable to attempt to regain a full range of movement at one session. Serial manipulations should be undertaken at intervals depending on the cause of the restriction of movement, the degree of co-operation of the patient in the performance of remedial exercises and the degree of reaction following the procedure. As a rule, not more than about 30% increase in range of mobility should be attempted at each session.

(3) *Osteo-arthritic joints:* (a) Containing adhesions following minor trauma, e.g. underlying internal lateral ligament of the knee. Such cases respond well to a single manipulation followed by active exercises.

(b) With contractures, e.g. flexed knees and flexed and adducted hips. Manipulation should be followed by corrective splinting and early physiotherapy, to encourage remedial exercises by relieving pain.

Hydrotherapy helps, especially exercises in the deep pool bath and contrast douching.

(4) *Rheumatoid joints with contractures:* Here manipulations must be guarded, and preferably serial. Not too much must be attempted at each manipulation and each must be followed by immediate splintage in the corrected position. Splints must be removable, i.e. split plaster, to allow daily active assisted movements—beginning within forty-eight hours of the manipulation—owing to the strong tendency for the development of intra-articular adhesions in these cases.

All manipulations should be performed under anaesthesia and great care taken not to fracture the decalcified bones.

(5) *Hysterical fixation of the joint*: Each case must be evaluated to make sure that the soft tissue contractures have not occurred to such a degree as to make a return of function impossible. If the joint does move freely under the anæsthetic, then a good result may be obtained, provided that strong suggestion is employed, particularly when the patient is just coming round from the anæsthetic and is especially susceptible to suggestion.

(6) *Cases where adhesions have taken place in tendon sheaths* or between tendinous aponeuroses and underlying joint capsules, e.g. adhesions in the sheath of the long tendon of the biceps, adhesions between the common extensor tendon of the forearm and the capsule of the elbow-joint ("tennis elbow") and adhesions in the tendon sheaths on the outer side of the foot.

Here better results are obtained by manipulation without anæsthesia, as the patient's instinctive muscular resistance to the movement provides the necessary counter-pull to break the adhesion.

*Essentials in manipulative technique.*—(1) Secure preliminary relaxation: (a) By anæsthesia; (b) without anæsthesia, by gaining the patient's confidence, placing him in a position to eliminate muscular tension, and using physical methods such as a hot bath, hot packs or a heat cradle to ensure a feeling of well-being and muscular relaxation. (2) Employ traction to separate joint surfaces: (a) By direct pull, e.g. neck and wrist; (b) by manœuvres which attain the same result indirectly; (c) downward pressure, in dorsal region, with patient prone, or rotary movement in case of lumbar spine with patient on his side. (3) First "take up slack", then a short, sharp thrust which is much more likely to be effective than a steady, forcing movement. (4) Movements at right-angles to plane of normal voluntary movement are most effective in breaking adhesions, as are quick rotary movements. (5) If muscular contractures are present, some time spent in kneading muscles at right-angles to their long axis is a helpful preliminary. (6) Precise knowledge of movement to be obtained.

*After-treatment.*—It is essential that the person who performs the manipulation should supervise the subsequent after-treatment. (1) The primary requisite is early active movement, not passive. (2) Muscle stiffness requires relief by hydrotherapy (exercises in deep pool) or by hot packs, radiant heat and gentle active massage. (3) Where adhesions have been dense, analgesics are called for to enable the patient to carry out the necessary active exercises that are essential for recovery of function.

*Dangers of manipulation.*—(1) Risk of lighting up a latent pathological process, (a) acute infective—especially in spontaneous hyperæmic dislocation of cervical spine. (b) chronic infective—e.g. tuberculous infection of bone and joint. (c) neoplastic—e.g. carcinomatous metastases in spine. N.B.—Pain of metastases often appears months before radiological changes. (2) Risk of fracture—especially in hyperæmic zone of decalcification, at level of synovial reflection in arthritic joints. (3) Risk of producing a dislocation by excessive force, especially in shoulder-joint. (4) Risk of producing a joint reaction by excessive force which leads to an increase in subsequent stiffness and consequently defeats the object of the manipulation.

Dr. E. J. Crisp: *Manipulation of the spine.*—Before the war it was customary to follow the axiom of the late Mr. W. H. Trethowan: "When in doubt, manipulate." Accordingly, manipulation was the order of the day for pain in the back at that time attributed to "fibrositis", "sacro-iliac strain", osteo-arthritis, "adhesions" and other conditions. The patient was anæsthetized and the joints of the spine put through their full range of movements, voluntary and involuntary. The possibility of the intervertebral discs being damaged by this procedure was overlooked, and the mechanics of the spine ignored. The surprising thing is that many cases were relieved by this vigorous treatment. Careful "follow-up", however, shows that the majority of cases relapsed sooner or later.

An intervertebral joint is a complex structure, consisting of two main components. Posteriorly, are the apophyseal joints which are diarthrodial; anteriorly is the joint between the vertebral bodies, which is a synchondrosis. Although it is perfectly safe to subject a diarthrodial joint to vigorous manipulation, it should be obvious that this type of treatment is inadvisable and may be dangerous for a synchondrosis.

Study of the anatomy, physiology and mechanics of the disc still further emphasizes the need for caution when manipulating the spine. The nucleus pulposus which forms the fulcrum for flexion and extension is situated somewhat posteriorly in the disc substance, especially in the lumbar and cervical regions. In consequence, the annulus is much thinner behind than in front. Furthermore, the nucleus pulposus which draws its fluid content from the spongiosa of the adjacent vertebrae by a process of osmosis, is contained within the annulus under considerable pressure, even when the individual is at rest. Hence, flexion of the lumbar spine which tends to squeeze the nucleus backwards, must impose considerable strain on the annulus posteriorly.

The axis for rotation is situated posterior to the thecal canal at the junction of the laminae (Capener [1]). This makes it evident that rotation must subject the discs to considerable distortion.

The intervertebral discs are never at rest, but always actively functioning. In consequence, they degenerate earlier and more rapidly than most other bodily structures. The investigations of Coventry, Ghormlie and Kernohan [2] on cadavers showed that in the lumbar region degeneration began as early as the third decade of life. During the fourth decade fissuring, hyaline degeneration and vascularization of the annulus were frequently observed, and by the sixth decade posterior rupture of the annulus had occurred in a large proportion of cases.

Correlation of these facts makes it evident that forced flexion or rotation of the spine is fraught with danger, especially in the lumbar and cervical regions, the only permissible manipulations being traction, extension and lateral flexion. In the dorsal region where the nucleus is more centrally placed and the thoracic cage affords additional protection, forced rotation is permissible provided it is localized to the dorsal spine.

*Indications for manipulation and technique.* (a) *Lumbar region:* A deranged disc is now recognized as the usual cause of pain in the back and responsible for symptoms previously designated as "fibrositis", "sacro-iliac strain" or "adhesions", while osteo-arthritic changes are also regarded as indicative of a deranged disc. Ligamentous or myofascial injuries giving rise to adhesions are rare occurrences, rupture of a disc almost always occurring first. Accordingly, there are few indications for manipulating the lumbar spine, as disc lesions in this region recover satisfactorily if the spine is immobilized in a plaster jacket. A few practitioners claim that it is safe and easy to reduce a disc protrusion by manipulation. The procedure is carried out without anaesthesia and with the patient lying prone. The operator after lifting the thighs with one hand, and thus hyperextending the spine, gives a thrust over the affected segment with the other hand. It would appear rational to follow a successful manipulation by applying a plaster jacket to allow the lesion to heal. The recurrence rate should then be considerably less.

Cases of residual sciatic pain, where a ruptured disc has clinically healed, and in which the symptoms may reasonably be attributed to an adherent nerve root, may sometimes be completely relieved by epidural injection followed by ham-string stretching.

In general, lumbar pain secondary to a disc lesion is best treated by rest; manipulation, if any, should be limited to traction, lateral flexion and extension.

(b) *Cervical region:* Many painful cervical conditions and associated brachial pain are directly attributable to injury or degeneration of one or more lower cervical intervertebral discs. There are two main clinical types: (1) Acute protrusion of a cervical disc with a flattened or reversed cervical curve, and little or no osteo-arthritic changes. (2) Cases in which osteo-arthritic changes and narrowing of the discs are already well marked at the time of the first onset of pain.

Most cases recover satisfactorily if rested and treated with short-wave diathermy, but it is often possible to cut short the attack by a judicious manipulation. As in the lumbar region, so in the cervical region the manipulations should be limited to traction, lateral flexion and extension. Traction is the most effective method. It may be carried out with the patient sitting or lying, but the former method is preferable, as the weight of the patient's body does most of the work. If the patient is unable to relax satisfactorily distraction may be performed under anaesthesia. An alternative method is to treat the patient by head suspension, which may be carried out daily.

(c) *Dorsal region:* Dorsal disc lesions do occur and are a rational explanation of severe dorsal pain and intercostal neuralgia. Cases of this type may be rapidly relieved by manipulation, the methods employed being traction, extension and rotation. The manipulation is best performed on the high ride plinth, care being taken when carrying out forced rotation to fully extend the lumbar spine and thus localize the movement to the dorsal region.

#### REFERENCES

- 1 CAPENER, N. (1944) Sciatica, *Ann. Rheumat. Dis.*, 4, 29.
- 2 COVENTRY, M. B., GHORMLIE, R. K. and KERNOHAN, J. G. (1945) The intervertebral disc—its microscopic anatomy and pathology, *J. Bone Jt. Surg.*, 27, 233-247; 460-474.

**Dr. Guy Beauchamp:** It is advisable that manipulative treatment for cervical lesions should be performed with the patient in the sitting position; the patient's body-weight may thus be used as a means of traction. Greater control can be achieved than with the patient in the recumbent position, for the operative hand moves through a shorter distance and distraction is effortless against the patient's sagging body-weight.

In lumbar disc lesions manipulation still has its uses in treatment, but it must be remembered, as Dr. Crisp has pointed out, that since extension is necessary for comfort, all manipulative procedures must be carried out in this position. Any manipulative measure that forces the spine into flexion is dangerous, and will exaggerate the disability.

Where it is not possible to give rest in bed, or to apply a plaster, I have found that rhythmic traction on an extension table with extension thrusts at the peak of extension may reduce the disc propulsion.

**Mr. W. D. Coltart:** Manipulations are performed for three reasons, to correct deformities, to reduce displacements of intra-articular structures, and to relieve pains which may or may not be associated with a limitation of movement. Considering the last group alone, a successful manipulation means that we have ruptured adhesions which have been painful when stretched. I believe that the mechanics of manipulation are as simple as that. If our manipulation is not successful in relieving pain it means that the adhesions have not been ruptured either because they are too tough, or too deep, or because there are too many of them. Sometimes we fail because our technique is at fault.

**Mr. W. E. Tucker:** Dr. Crisp has mentioned the importance of obtaining the full range of involuntary movements as well as voluntary ones. This confirms the teaching of Dr. James Mennell who emphasized the following basic principles of manipulation:

(1) Traction and countertraction so that joint surfaces are separated, in order to overcome any contraction of capsule, ligaments, and overlying soft tissues.

(2) Involuntary movements of joint whilst traction and countertraction are maintained—this allows for free rotating and gliding movements in the joint.

(3) Full active movements whilst still maintaining traction and countertraction.

Mr. Bastow has stressed the importance of gentle frequent manipulations. Even where manipulations are done under anaesthesia there should be careful control of any forcing in order to prevent excessive reaction.

In cases where limitation of movement from adhesions, and marked muscle wasting and inflammatory oedema are also present, it is wiser, before considering forcible manipulations under anaesthesia, to undertake a series of gentle manipulations daily combined with faradism and massage whilst the patient takes regular contrast baths and does exercises.

Reaction to manipulation must never be excessive or adhesions will re-form before the products of reaction can be dispersed.

In manipulating for contracted muscle following a tear, it must be remembered some muscles act through and on two joints: the proximal joint must be fixed in the position which puts the muscle on the stretch, and then the distal joint is put through the range of movements which further stretches that muscle, e.g. the rectus femoris flexes the hip-joint and extends the knee: when manipulating to stretch, fix the hip-joint in full extension before flexing the knee fully.

*Special joints.*—(a) *Ankle:* In a severe sprain the tibia may ride forward on talus and a true subluxation occurs. In manipulating it is essential to push the tibia backwards on the talus. Chronic sprain of the posterior fibres of the external lateral ligament shows itself as pain and limitation of movement on forcing abduction of the forefoot. To stretch this ligament, forcibly abduct the forefoot while the counter-thrust is placed on the outer side of the heel in an inward direction.

(b) *Shoulder:* Frozen shoulders usually benefit by several weeks of physical treatment, heat, massage, faradism, with gentle manipulation before forcible manipulation. Where this is contemplated full internal rotation is best accomplished by turning the patient on to the opposite side, the manipulator bringing the affected arm slowly up the back with one hand whilst the other hand holds and steadies the head of the humerus thus obviating the risk of dislocation.

(c) *Back:* Disc injuries—very gentle manipulation combined with anodal galvanism, heat, massage and gentle faradism overcomes muscle spasm and sometimes gets the patient symptom-free in a few days. Subsequent treatment depends on active requirements of patient. In some cases a plaster jacket may be necessary; in other cases a belt or orthopaedic felt pad and elastic webbing. Failing quick recovery complete rest in bed may be necessary. To prevent recurrence development of abdominal muscles and flexors of spine is as important as extensors; in the act of flexion and extension these protect the fronts of the vertebral bodies and help to prevent the disc from being protruded posteriorly.

Finally, cine-radiography as developed by Dr. Russell Reynolds is opening up a new field which will help to put manipulative surgery on a sound scientific basis.

## Section of Otology

President—R. SCOTT STEVENSON, F.R.C.S.Ed.

[December 3, 1948]

### Extensions of the Tympanic Cavity. [Summary<sup>1</sup>]

By Professor VICTOR LAMBERT, F.R.C.S.Ed.

THE most cursory examination of the base of the skull of, say, a Lemur and a Homo reveals at once the striking fact that the bulla, which is such a conspicuous feature of the lemurine skull, is completely absent in Homo, but that in Homo the area previously occupied by the bulla is honeycombed with small air-containing spaces which we recognize as pneumatization. Professor F. Wood-Jones suggested to me that an examination of the temporal bones of the Primates might help to elucidate the underlying mystery of this change, particularly as it was felt that the structural changes must, as in all cases, be a reflection of changed functional need.

In the investigation it was decided not to consider the various cranial elements forming the tympanic cavity or their phylogenetic origin, particularly as this field had already been well covered by many previous writers. Consideration was given to the evolution of the ossicular chain, but as this was done from literature and not by original observation, it is not included in this paper.

When the lower vertebrates which were formerly wholly aquatic in their habits became even partially terrestrial, a new method of conducting sound waves to the ear was necessitated, and so the eustachian tube, the tympanic cavity, and the external auditory meatus were developed. It would seem that from the first inception of a mechanism to deal with air-borne sound waves, there developed a resonance chamber intervening between the membrana tympani or its homologue and the internal ear, and that this resonance chamber was essentially a dilatation of the posterior end of the eustachian tube. This posterior dilatation we are accustomed to call the bulbus eustachii. In the primitive land-living vertebrates, it is a comparatively small cavity, the limits of which are defined by the area occupied by the membrana tympani on the one hand, and the immediate region of the fenestra ovalis and the fenestra rotunda on the other.

In the very lowest of the marsupial mammals a marked advance from this condition is met with; there is still the tympanic cavity of the lower vertebrates which is represented by what we term here the atrium, but in addition to this the cavity is enlarged by an apparently new dilatation of the bulbus eustachii. This is the cavity which in mammalian anatomy is referred to as the auditory bulla. The development of this added resonance chamber appears to be a necessity in all the lower animals regardless of their phylogenetic relations, and in the different phyla the chamber is formed by such varied cranial elements as the entotympanic, the petrous, the sphenoid and the squamosal.

In all these primitive mammals the internal carotid artery is a comparatively small vessel, greatly exceeded in size by the external carotid artery, but in the primitive mammals the large cranio-facial area derives its blood supply from the external carotid artery, whilst the smaller of the two vessels, the internal carotid artery, supplies the brain, which at this stage is relatively small. In the different mammalian types, the internal carotid artery enters the skull in a variety of ways. In the Primates alone does the site of entry eventually happen to coincide with the area from which the bulla is derived, but so long as the internal carotid artery remains small, there is no embarrassment to the bulla, but when the carotid artery increases in size, it eventually usurps the area occupied by the bulla.

Fig. 1 shows the bulla of Tarsius, which it will be seen greatly exceeds the size of the atrium proper, and the carotid canal is present as a thin tube of bone passing through the posterior margin of the bulla.

In fig. 2, the Old World Monkey, we see the greatly increased internal carotid artery passing through the apex of the petrous bone, and no sign of bulla development can be recognized on the surface of the skull. The homologue of the bulla is now apparently nothing more than a pneumatized area in the petrous apex, which communicates in a rather variable way with the extremity of the tympanic tube. This condition of a variably pneumatized petrous apex is maintained in all the Old World Monkeys, Anthropoid Apes, and Man. In Man, the communication between the eustachian tube and pneumatic cells of the petrous apex takes place in a variable manner. It is apparently normal in Man for some diverticula of the tube to be developed from its lower surface at its mesial extremity. These represent

<sup>1</sup>The full paper will appear in the *Journal of Laryngology and Otology*.

the "tubal cells" which were shown in the corrosion specimens of the middle ear by Siebenmann, quoted in Poirier's book in 1912 (POIRIER, P., and CHARPY, A., *Traité d'anatomie humaine*, Paris, 2nd edit., 5, ii).

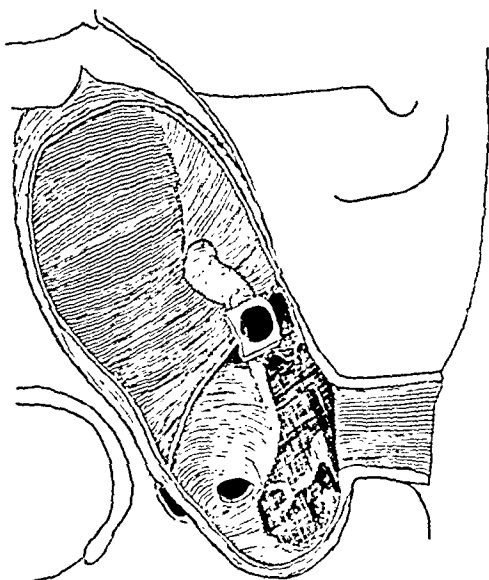


FIG. 1.—Left bulla of *Tarsius* opened from below.



FIG. 2.—Under side of the right tympanic region in the skull of an adult *Papio*. The petrous apex has had its lower surface removed. The external auditory meatus has been removed and the atrium is exposed. The posterior portion of the temporal has been opened to display the pneumatization.

Fig. 3 graphically illustrates the effect of the ever-increasing size of the internal carotid artery on the bulla area. It is probable that the antagonism between the development of a large internal carotid artery and the formation of the bulla chamber in the area of bone that it invades is capable of a functional explanation. In the Primate series, the internal carotid artery is an ever-increasing vessel, because of the demands of an increased blood supply to an ever-increasing brain. In the final stages, when the typical development of the cortex characteristic of the higher Primates is achieved, the internal carotid artery has usurped the whole of the area in which the primitive mammalian bulla is developed.

It would seem justifiable to imagine that a reduction of the resonance chamber connected with the tympanic cavity and the enlargement of cortical auditory areas might have been a harmonious process in the development of the Primates. Mere auditory acuity, as Cuvier postulated, is of the utmost importance as a life-saving mechanism in more primitive nocturnal animals, to which even the slightest sound is their principal warning. The cortical sense of this sound-receiving mechanism need not be, and in fact is not, at all extensive. The auditory sense organ of the lower animals may be described as a mechanism developed for a quantitative appreciation of sound waves, of which the cortical connotation need not necessarily be pondered. On the other hand, in the Primates with their ever-increasing cortical area devoted to the psychological appreciation of sound, the actual efficiency of the end-organ need not necessarily be so great; indeed, the story that applies to other sense organs of the Primates seems to be true in the case of the ear. For survival importance, the cortical interpretation of any sensory impulse vastly outweighs the perfection of the sensory receptor.

Some slight anatomical evidence of this in the case of the ear may be obtained by contrasting the brains of the New and the Old World Monkeys (fig. 4), for it is here seen that the part of the brain connected with subcortical reception of auditory impulses is the inferior corpus quadrigeminum, and it would be natural to suppose that this body might be better developed in animals that had an efficient area of cortical representation. In contrasting the inferior corpora quadrigemina of the New and the Old World Monkeys it is found that in the

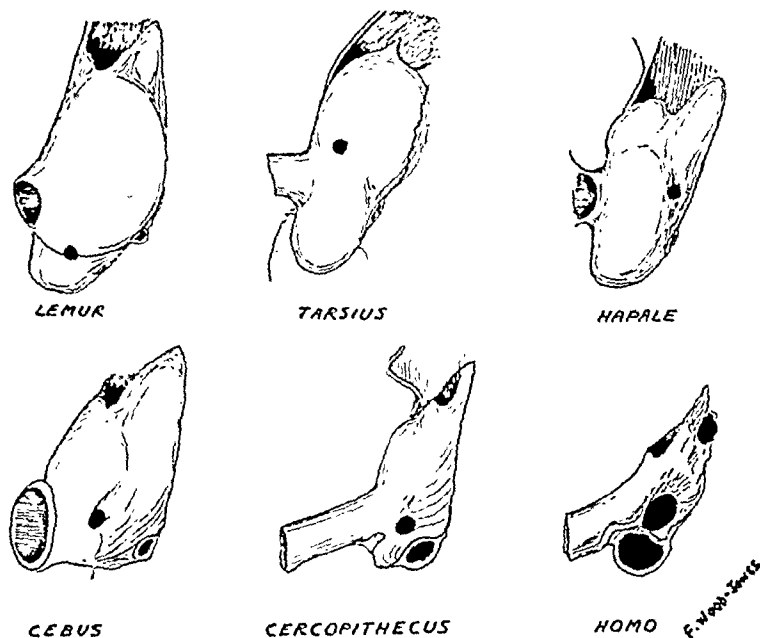


FIG. 3.—Right bulla region of a series of Primates to show the relations of the carotid artery, jugular vein, and eustachian tube to the bulla region.



(a)

(b)

FIG. 4.—Right side of the mid-brain of (a) Platyrrhine and (b) Catarrhine monkey of similar size. The cerebellum and posterior part of the hemispheres have been removed to show the corpora quadrigemina. In the Platyrrhine, the inferior corpus quadrigeminum considerably exceeds the size of the superior body. In the Catarrhine, the inferior corpus quadrigeminum is relatively smaller and is about equal in size to the superior body.

New World Monkeys, where the bulla development and epitympanic extensions are still present, the inferior corpora quadrigemina considerably exceed the superior bodies in size, whereas in the Old World Monkeys, where the bulla region and the posterior extensions are practically obsolete, the reverse is true.



the "tubal cells" which were shown in the corrosion specimens of the middle ear by Siebenmann, quoted in Poirier's book in 1912 (POIRIER, P., and CHARPY, A., *Traité d'anatomie humaine*, Paris, 2nd edit., 5, ii).

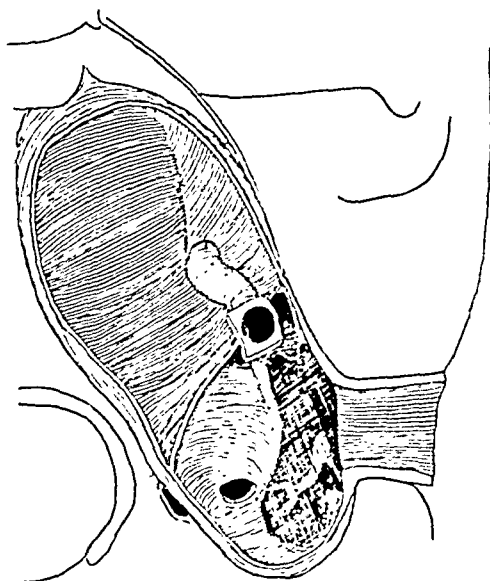


FIG. 1.—Left bulla of *Tarsius* opened from below.



FIG. 2.—Under side of the right tympanic region in the skull of an adult *Papio*. The petrous apex has had its lower surface removed. The external auditory meatus has been removed and the atrium is exposed. The posterior portion of the temporal has been opened to display the pneumatization.

Fig. 3 graphically illustrates the effect of the ever-increasing size of the internal carotid artery on the bulla area. It is probable that the antagonism between the development of a large internal carotid artery and the formation of the bulla chamber in the area of bone that it invades is capable of a functional explanation. In the Primate series, the internal carotid artery is an ever-increasing vessel, because of the demands of an increased blood supply to an ever-increasing brain. In the final stages, when the typical development of the cortex characteristic of the higher Primates is achieved, the internal carotid artery has usurped the whole of the area in which the primitive mammalian bulla is developed.

It would seem justifiable to imagine that a reduction of the resonance chamber connected with the tympanic cavity and the enlargement of cortical auditory areas might have been a harmonious process in the development of the Primates. Mere auditory acuity, as Cuvier postulated, is of the utmost importance as a life-saving mechanism in more primitive nocturnal animals, to which even the slightest sound is their principal warning. The cortical sense of this sound-receiving mechanism need not be, and in fact is not, at all extensive. The auditory sense organ of the lower animals may be described as a mechanism developed for a quantitative appreciation of sound waves, of which the cortical connotation need not necessarily be pondered. On the other hand, in the Primates with their ever-increasing cortical area devoted to the psychological appreciation of sound, the actual efficiency of the end-organ need not necessarily be so great; indeed, the story that applies to other sense organs of the Primates seems to be true in the case of the ear. For survival importance, the cortical interpretation of any sensory impulse vastly outweighs the perfection of the sensory receptor.

Some slight anatomical evidence of this in the case of the ear may be obtained by contrasting the brains of the New and the Old World Monkeys (fig. 4), for it is here seen that the part of the brain connected with subcortical reception of auditory impulses is the inferior corpus quadrigeminum, and it would be natural to suppose that this body might be better developed in animals that had an efficient area of cortical representation. In contrasting the inferior corpora quadrigemina of the New and the Old World Monkeys it is found that in the

(2) The ætiological factor is cold, though water itself, at higher temperatures, may produce some effect.

(3) Exostoses may be present in susceptible individuals after three years of regular swimming, the shortest period in this series being after two years' exposure, in a boy of 14.

(4) Insufficient evidence was available to assess the possibility of the presence of associated middle-ear exostoses as a cause of deafness in swimmers.

#### REFERENCES

- FIELD, G. P. (1893) *Diseases of the Ear*. London, Fourth Ed., p. 83.  
 VAN GILSE, P. H. G. (1938) *Acta Oto-Laryng.*, 26, 343.

Mr. H. V. Forster said that his experience agreed with that of Mr. Adams that these cases were less commonly observed in the hospital clinic. He remembered well a number seen privately in the consulting room which included players of water polo and enthusiastic amateur swimmers.

He had occasionally noted hyperostoses in patients with chronic suppurative otitis media treated regularly at home with the syringe, but it was difficult to be certain that the treatment had been the cause of the bony changes in the external auditory canal.

Mr. N. A. Punt said that amongst the troops in Austria and North Italy nearly all the men were very keen swimmers, and amongst them was found a relatively large incidence of exostoses of the external auditory canals, in marked contrast with the rarity of such conditions among men who did not swim, such as the rural population of mid-Kent.

There might be some analogy with exostosis of the tibia occurring in cases of varicose ulcer, which present the sequence of skin irritation, periosteal irritation and exostosis.

Mr. Graham Brown thought that the association with exostosis of inflammation of the external auditory canal was a very real thing. A great number of people who went swimming got otitis externa, and he thought that the association of inflammation of the canal, the effect of wax, and of the water, together with infection, created a very favourable condition for irritation and inflammation of the bony meatus. This was seen particularly in tropical and subtropical regions where a great proportion of the population commonly bathed. In his view the great ætiological factor in the formation of exostosis was the inflammatory condition produced by water in the ear, whether fresh or salt, which in turn led to a periostitis and deposit of bone.

Mr. R. R. Simpson said that he spent three years in Ceylon during the war where he had records of over 6,000 cases of otitis externa. Among the men there, who were accustomed to frequent bathing, otitis externa was extremely common and exostoses extremely rare.

Mr. W. I. Daggett agreed with Mr. Simpson's experience after his own two years in the Mediterranean.

Mr. Stirk Adams, in reply, said that in his own series the earliest sign of exostoses was encountered in a school boy who had been swimming regularly for two years, while most of these boys had been swimming regularly for at least three years, and others from four to eight years. In Van Gilse's series, exostoses were recognized after eight months' exposure to regular swimming, and one year after continuous use of cold aural drops.

## Demonstration of the Human Labyrinth and its Related Structures in Perspex

By OLIVER GRAY, M.B.E., B.A., M.B., Ch.B.

A BRIEF outline of the method of preparation was given, a full description of which will be found in the *Journal of Laryngology and Otology* for May 1948. It was pointed out that this was based upon the pioneer work of the late Dr. A. A. Gray of Glasgow (father of Dr. Oliver Gray).

Monomeric methyl methacrylate, "the monomer", is a liquid of the consistency of water which, under the influence of heat or ultraviolet light, becomes polymerized into a hard solid, "the polymer". This latter substance is known as Perspex and is as clear as glass. After complete dehydration the portion of the temporal bone is placed in the liquid monomer which invades all the tissues *except* the dense bone. Gentle heat is then applied and the monomer "sets". Eventually everything that is not bone becomes impregnated with solid Perspex. Now it so happens that Perspex is quite unaffected by strong hydrochloric acid,

Why the bulla area should be replaced by pneumatization is one of the unsolved problems in comparative anatomy, and this investigation has not helped to solve it, but it would appear that the bulla mechanism is rendered obsolete by the growth of the central critical faculty of the brain.

The reproductions are photographs of the original black and white drawings which Professor Wood-Jones was kind enough to make for me.

## The Ætiology of Swimmers' Exostoses of the External Auditory Canals and of Associated Changes in Hearing [*Résumé*]

By W. STIRK ADAMS, F.R.C.S.

THIS enquiry was undertaken to ascertain whether the opinion held by English Otologists of the last century, particularly G. P. Field (1893), and later by Van Gilse (1938) and Belgraver (quoted by Van Gilse) of Leyden, that massive exostoses of the external auditory canals were the result of long-continued swimming was still valid; and if this was supported, to discover the causal factor in swimming producing these changes, and to ascertain the incidence of deafness in their presence, as an indication of possible associated exostoses in the middle ear.

During the past five years every patient in whom external canal exostoses have been observed in my practice has been asked for a history of swimming. The questionnaire included the family liability to deafness, the age at which swimming was learned, the number of years during which it was practised, either occasionally or regularly, in baths, river or sea. It included the swimming stroke used, the practice of diving or plunging, swimming under water, and the habit of immersing the head when taking hot or cold baths, and the use of a rubber head protector.

In all, 22 men and 6 women presented exostoses, and all gave a history of regular practice of swimming. The ages of the men ranged between 22 and 57, and they began to swim at between 5 and 14 years old, while their swimming history was from 6 to 41 years. The ages of the women ranged between 17 and 44. They had learned to swim at between 5 and 12 years old and their swimming history extended from 10 to 33 years.

In these 28 patients social deafness was only present in 6, and in 4 of these a family liability to deafness was recorded.

Of the swimming strokes used, the breast stroke predominated. Diving and swimming in fresh or salt water, either in the tropics or in England, appeared to have little influence on the size of the exostoses present.

In the course of this enquiry, however, other patients suffering from deafness who had no exostoses gave a swimming history, and it became evident that only a proportion of those exposed to similar risks developed these bony changes.

To estimate this proportion I examined in 1947 the ears of 18 boys aged 13 to 19 years, who were members of a public school swimming team, with a swimming history of from two to eight years. Of these, 14 showed evidence of exostoses, while 4 had normal canals. As a control, 11 school non-swimmers of the same age-group were examined, and of these only two showed deviations from the normal symmetry; one of them immersed his head in hot water baths; the other had no water history at all.

In assessing the ætiological factor in susceptible individuals the effect of hypertonic and hypotonic solutions was considered, and also the possibility of a surge of water in wide canals. I reached the conclusion that the stimulus of cold some 35° F. below body temperature is chiefly responsible. This view is supported by two other cases of exostoses in men who were not regular swimmers. One aged 64, with bilateral occluding exostoses, had immersed his head in a daily cold bath since boyhood; while the other, aged 68, had rolled his head under hot water in a daily bath all his life. He presented, on one side only, two minute exostoses external to the upper part of the tympanic ring.

### CONCLUSIONS

(1) The enquiry confirmed the views of Field and Van Gilse that massive exostoses of the external auditory canals are the result of swimming.

## Section of Orthopædics

President—H. J. SEDDON, M.A., D.M., F.R.C.S.

[February 1, 1949]

### The Practical Value of Peripheral Nerve Repair

#### PRESIDENT'S ADDRESS

By H. J. SEDDON, M.A., D.M., F.R.C.S.

THE time has come when those of us who have had the privilege of dealing with peripheral nerve injuries during the war should give some account of our stewardship. The work of the five main centres will shortly be presented in a report to the Medical Research Council, but there is something to be said for epitomizing some of the practical conclusions.

In spite of all that has been written on peripheral nerve injuries there is little to tell the surgeon precisely when to operate, and what sort of result he may reasonably expect from suture in any particular circumstances. Current opinions about the results of surgical repair range from the uncritical claims of those who have performed primary sutures with what they call perfect results, to the views of some pessimists who consider that the only serviceable treatment for sciatic palsy is a below-knee amputation, and for high ulnar palsy, amputation of the little finger. The truth, of course, lies somewhere between these extremes.

The history of peripheral nerve surgery during the last thirty years may be briefly summarized in the following way. During the First World War surgeons, especially in this country, advanced the technique of secondary suture to something little short of perfection; the closure of large gaps after free mobilization of the nerve stumps and flexion of the appropriate joints became completely standardized; for all but clean incised wounds secondary suture was regarded as the treatment of choice. However, there was still a belief, which persists to this day, in the great superiority of primary suture where conditions permit its employment. Nerve grafting of every sort was condemned as useless. Between the wars Ballance and Duel (1932) showed that grafting of the facial nerve was not merely feasible but actually reliable. Bunnell (1927) had some success in grafting severed digital nerves and later, in a few cases of extensive injury of large nerve trunks, he recorded (Bunnell and Boyes, 1939) successes after the implantation of cable grafts. After the First World War there was much discussion of the results of nerve suture but it was mostly unfruitful and for this there were two reasons. There were no agreed criteria for assessment of the various grades of recovery and such terms as *excellent*, *good* and *fair* had almost as many meanings as there were surgeons using them. What is more, very few cases were followed regularly for a sufficient length of time, and it is, I think, fair to say that the only report that would satisfy present-day criteria was that made by Stopford before this Society (1920*a* and *b*).

In the small group of cases which have been demonstrated to this meeting it is reasonable to describe recovery as satisfactory,

Thanks to the co-operation between all the men working at the British centres, these and the less satisfactory grades of recovery have been dispassionately assessed according to fairly simple criteria; and it is my aim to indicate how frequently the sort of recovery that you have seen in these deliberately selected cases may be expected, and what steps should be taken for obtaining it.

#### RESULTS OF SUTURE

I shall give, first, the results of suture from my own centre (Table I); the combined figures for the five centres will appear later in the M.R.C. Report. Tables II and III indicate how the results are assessed. The basis of this classification is and must be

and when the whole is subsequently placed in the acid bath, the bone is dissolved away, gradually disclosing, with singular completeness and fidelity, the component structures of the ear. The photograph (fig. 1) illustrates the results which can be achieved by this process.



FIG. 1.—Photograph of right labyrinth (human) and related structures in polymerized methyl methacrylate (Perspex) after removal of the dense bone by hydrochloric acid. Viewed from above.

- A. External auditory meatus
- B. Facial canal
- C. Mastoid antrum
- D. Lateral canal
- E. Superior canal
- F. Nerve to superior and lateral ampullae
- G. Aqueduct of the vestibule

- H. Geniculate ganglion
- I. Internal auditory meatus
- J. Carotid artery
- K. Great superficial petrosal nerve
- L. Lesser superficial petrosal nerve
- M. Eustachian tube
- N. Nerve from tympanic plexus
- O. Chorda tympani

Owing to the durable nature of the Perspex, the relationship of the delicate structures is permanently preserved in such a way that a precise study can be made of one of the most intricate parts of human anatomy and, with reasonable care, the specimens can be handled without fear of damage.

This new method may also help us in challenging the textbook descriptions, which are none too secure. For instance, the fact that the chorda tympani does not leave the skull through the petrotympanic fissure (Gray, "Atlas of Otology") is shown clearly in the preparations obtained in this way.

At the meeting of the Section, in the morning, lantern slides were shown, and throughout the day an opportunity was given of viewing the specimens.

#### REFERENCES

- GRAY, A. A. (1924) *Atlas of Otology*. Glasgow.
- GRAY, O. (1948) New method of demonstrating the labyrinth, *J. Laryng. Otol.*, 62, 308.

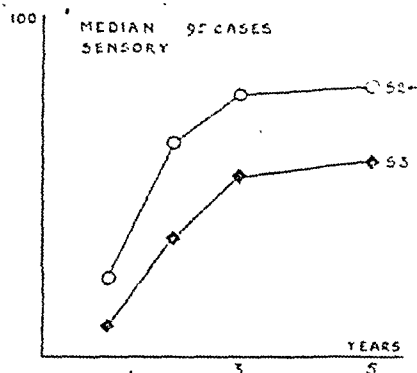


FIG. 3.—Median nerve: sensory recovery. Recovery to S2 + is sufficiently useful to warrant operation. The proportion of useful recoveries is, therefore, high—79.4%

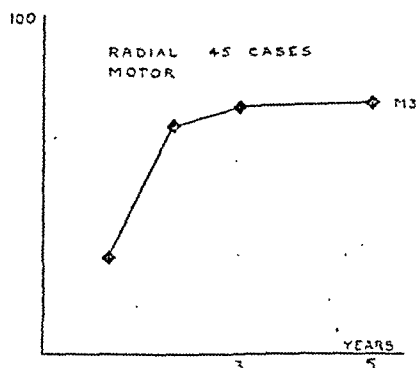


FIG. 4.—Radial nerve: motor recovery.

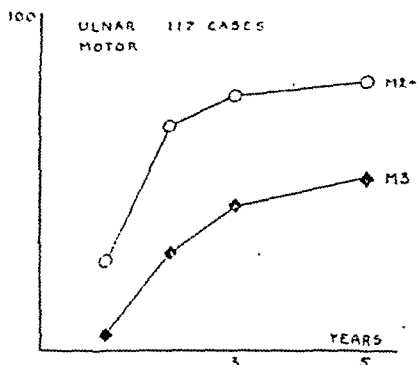


FIG. 5.—Ulnar nerve: motor recovery. Recovery to M2 + is sufficiently useful to warrant operation. The proportion of useful recoveries is, therefore, high—79.7%.

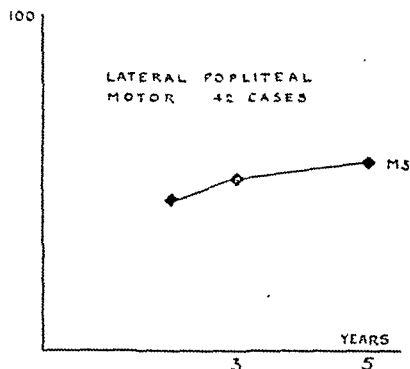


FIG. 6.—Lateral popliteal nerve: motor recovery. Nothing less than recovery to M3 enables the patient to dispense with a toe-raising spring.

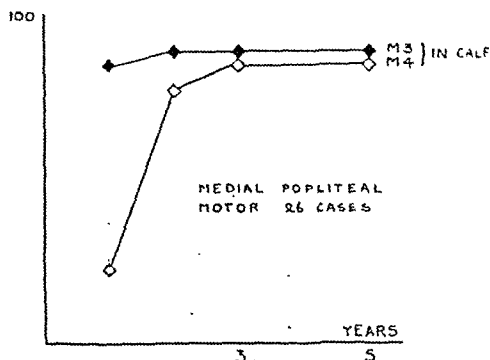


FIG. 7.—Medial popliteal nerve: motor recovery in calf. There is an astonishingly high proportion of good (M3) and very good (M4) recoveries. In some cases tibialis posterior also recovered but no return of power has yet been seen in the long flexors of the toes.

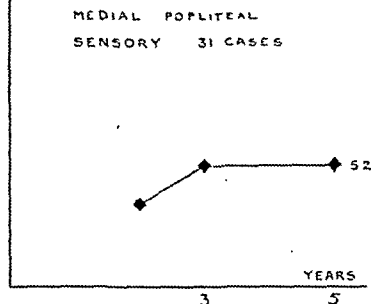


FIG. 8.—Medial popliteal nerve: sensory recovery. A depressing record: in no case was there recovery to S3, though recovery to S2 is sufficient to protect the sole against noxious stimuli and is usually compatible with good function.

The poor sensory recovery is in striking contrast with the good recovery in the calf and is due to the far greater distance that the outgrowing sensory axons have to travel.

strictly neurological. The results in terms of usefulness are often significantly different since, as Russell Davis (1949) has recently shown, the use that is made of the injured part is determined almost as much by the personality of the individual as by the quality of the motor and sensory recovery.

The method of presenting results, which was devised by R. B. Zachary, is the only

TABLE I.—CASES OF SUTURE AND PERIODS OF POST-OPERATIVE OBSERVATION  
Number examined at each anniversary

| Nerve             |    |    |    | Number examined at each anniversary |     |     |         |
|-------------------|----|----|----|-------------------------------------|-----|-----|---------|
|                   |    |    |    | 1                                   | 2   | 3   | 5 years |
| Ulnar             | .. | .. | .. | 117                                 | 109 | 88  | 88      |
| Median            | .. | .. | .. | 95                                  | 85  | 84  | 84      |
| Radial            | .. | .. | .. | 45                                  | 40  | 30  | 31      |
| Lateral popliteal | .. | .. | .. | 42                                  | 42  | 41  | 41      |
| Medial popliteal  | .. | .. | .. | 31                                  | 28  | 26  | 26      |
|                   |    |    |    | 330                                 | 304 | 269 | 270     |

The two divisions of the sciatic nerve have been considered separately throughout.

TABLE II.—MOTOR RECOVERY

- Stage 0 No contraction.  
 Stage 1 Return of perceptible contraction in the proximal muscles.  
 Stage 2 Return of perceptible contraction in both proximal and distal muscles.  
 Stage 3 Return of function in both proximal and distal muscles of such an extent that all important muscles are of sufficient power to act against resistance.  
 Stage 4 Return of function as in Stage 3 with the addition that all synergic and isolated movements are possible.  
 Stage 5 Complete recovery.

TABLE III.—SENSORY RECOVERY

- Stage 0 Absence of sensibility in the autonomous zone.  
 Stage 1 Recovery of deep cutaneous pain sensibility within the autonomous zone of the nerve.  
 Stage 2 Return of some degree of superficial cutaneous pain and touch sensibility within the autonomous zone of the nerve.  
 Stage 3 Return of superficial cutaneous pain and touch sensibility throughout the autonomous zone with disappearance of any over-response.  
 Stage 4 Return of sensibility as in Stage 3 with the addition that there is recovery of two-point discrimination within the autonomous zone.

satisfactory one I know. The day of operation is regarded as zero, the neurological results are assessed on the first and succeeding anniversaries, and the proportion of the number of cases available for assessment at each anniversary in which useful recovery has occurred is given as a percentage. Here are the results of suture of all the major nerve trunks, except the brachial plexus (figs. 1 to 8).

Throughout the figures, M3 and S3 have been regarded as satisfactory grades of recovery.

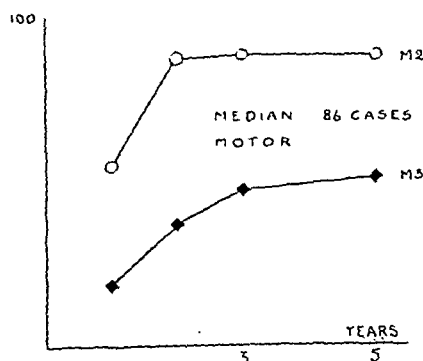


FIG. 1.

FIG. 1.—Median nerve: motor recovery. After a high median lesion recovery to M2 is useful, since it indicates that there is good power in the long muscles. Thus, in the whole series, useful motor recovery was obtained in 88%.

FIG. 2.—Median nerve: motor recovery. Low proportion of recoveries after repair of proximal lesions; high proportion after intermediate and distal lesions.

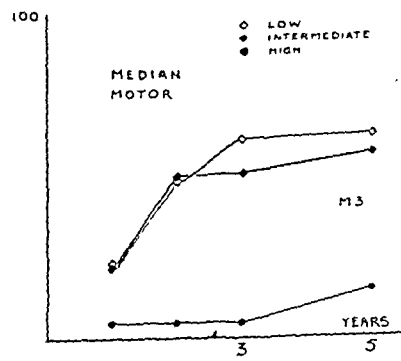


FIG. 2.

apparent. Even if repair is undertaken very early the axons cannot reach the periphery until many months have elapsed, by which time adverse changes in the peripheral stump, end-organs and muscle are well advanced and to some extent irreversible.

But one is occasionally faced with a case in which a very long delay has already occurred and the question then is whether it is worth while attempting repair. Zachary has worked out what may be called the *critical delay* (Table IV), that is to

TABLE IV.—CRITICAL DELAY (MONTHS)  
Based on Data from All Centres

|                  |         |               |    | High                     | Intermediate | Low |
|------------------|---------|---------------|----|--------------------------|--------------|-----|
| Median           | {       | Motor .. ..   | 9  | 13                       | 32           |     |
|                  |         | Sensory .. .. | 12 | 36 (child)<br>17 (adult) |              |     |
| Ulnar            | .. .. . | 12            | 16 | 18                       |              |     |
| Radial           | .. .. . | 13            | 16 | 16                       |              |     |
| Lat. popliteal   | .. .. . | 12            | 13 | 13                       |              |     |
| Medial popliteal | {       | Motor .. ..   | 13 | 15                       | 15           |     |
|                  |         | Sensory .. .. | 15 | 15                       | 15           |     |

say, the longest interval between injury and operation compatible with useful recovery. This, of course, is not to say that recovery can be promised, only a possibility of it sufficient to justify operation.

(3) *Extent of the gap*.—The closure of large gaps by end-to-end suture after extensive mobilization of the stumps was so welcome an advance that the only limitation recognized was whether it was anatomically possible to perform the operation. At Oxford, at the beginning of the war, we closed a number of large gaps, of the order of 12-15 cm., but in no single case did recovery occur. We then found that no one had ever investigated the fate of such cases. It was soon apparent (Highet and Holmes, 1943; Highet and Sanders, 1943) that the post-operative stretching needed to restore the posture of the limb to normal, however carefully performed, carried with it a grave risk of producing severe and extensive intraneural fibrosis indistinguishable from that seen after an acute traction injury. In short, it became evident that there is a biological limit, considerably stricter than the anatomical, to the extent of the gap that can safely be closed by mobilization and end-to-end suture. A new standard is necessary, which we have called the *critical resection length* (Table V).

TABLE V.—CRITICAL RESECTION LENGTHS (cm.)  
Based on Data from All Centres

|                |              |       | Based on Data from Air Centres |              |     |
|----------------|--------------|-------|--------------------------------|--------------|-----|
|                |              |       | High                           | Intermediate | Low |
| Median         | { Motor ..   | .. .. | 7                              | 8.5          | 7   |
|                | { Sensory .. | .. .. | 7                              | 9            | 7.5 |
| Ulnar          | .. ..        | .. .. | 10                             | 13           | 10  |
| Radial         | .. ..        | .. .. | 8                              | 8            | 7.5 |
| Lat. popliteal | .. ..        | .. .. | 9                              | 9            | 9   |
| Med. popliteal | .. ..        | .. .. | 10                             | 11           | 7   |

As a rough guide it may also be said that any suture requiring more than 90-100 degrees of flexion of the elbow or knee—the wrist should never be flexed even to that extent—carries a considerable risk of failure.

In the absence of any reliable alternative to end-to-end suture these figures would only be of prognostic interest, but since nerve grafting has emerged as a reliable alternative the determination of the critical resection length becomes a matter of immediate practical importance.

#### REVIEW OF THE CAUSES OF FAILURE

*Unavoidable Causes of Failure* may be quickly dismissed

(1) I have already mentioned the *proximal situation of the lesion*, which is particularly significant in injuries of the brachial plexus.



The next step is to determine what factors are responsible for failure to achieve a useful grade of recovery. Three stand out significantly.

(1) *The level of the lesion.*—The more proximal the lesion the worse the prognosis. This is well shown in fig. 2. There is one certain and another possible explanation of these poor results (*see* figs. 1, 2, 7 and 8). First, there is no doubt that the retrogressive changes in the periphery that impair the quality of recovery must be much more potent where the outgrowing axons have to travel a long way before reaching their destinations. It is also possible, though not yet proved, that the remarkable power of the neuron to synthesize and protrude a long stream of axoplasm has its limits. Where the axon of a very long neuron has been severed fairly near the cell body the latter is called on to produce a quantity of axoplasm many times its own volume, whereas after a distal lesion a much smaller effort suffices. The practical conclusion is that although useful recovery may occur after a high suture, the odds are against it; and in all lesions of the brachial plexus except those involving C.5 and 6 (Brooks, 1949) the results of suture are hardly good enough to warrant even an attempt at repair.

(2) *Delay.*—That delay in the repair of a severed nerve is harmful is generally admitted, but we must know how harmful it is and at what stage the effects of delay become such as completely to preclude a useful result after suture.

(a) The cellular bridge that conveys the outgrowing streams of axoplasm to the periphery is made up of Schwann cells and the adequacy of this bridge depends on their activity. Abercrombie and Johnson (1942) have shown in the rabbit (and the same appears to be true in man) that the activity of these cells reaches its peak at the third week after severance of the nerve and then declines progressively.

(b) The removal of the axonal and myelin remains from the peripheral stump—the chief feature of Wallerian degeneration—is followed by a progressive shrinkage of the peripheral Schwann tubes and an increase in the endoneurial collagen. At first this shrinkage is reversible but ultimately the tubes become so small that although they do not hinder the outgrowth of axons they do prevent their attaining an adequate diameter and the degree of myelination requisite for satisfactory function (Holmes and Young, 1942).

(c) The motor end-plates persist for some months but ultimately they disappear, and although regeneration is possible when re-innervation of a muscle occurs the new end-plates are very inferior structures (Gutmann and Young, 1944).

(d) The hindrances to late re-innervation of voluntary muscle are a consequence of the progressive atrophy and interstitial fibrosis of denervated muscle; the interstitial collagen offers actual physical obstruction to the outgrowing axons when they reach their destinations; and ultimately the atrophy of the muscle fibres may be such as completely to preclude recovery (Bowden and Gutmann, 1944).

(e) It is also likely, though not clearly proved, that similar harmful changes take place in the more elaborate of the sensory end-organs.

(f) A gross result of delay is shrinkage of the whole peripheral stump which makes it surgically impossible to obtain satisfactory apposition of the resected surfaces.

The conclusion is that the repair of a divided nerve should be undertaken with as little delay as possible, and to this end the healing of the wound and, where necessary, the replacement of a large cutaneous scar by healthy skin, should be expedited by every available means. And, so far as denervated muscle is concerned, atrophy should be controlled by daily stimulation with currents of sufficient duration to produce brisk contraction (Jackson and Seddon, 1945; Jackson, 1945). Nevertheless, as will be shown later, primary suture is still only a theoretical ideal.

One of the reasons why proximal lesions give relatively poor results is now more

was fair anatomical continuity. Later, we were able to compare the results of this expectant policy with those of suture of similar nerves at similar levels, and it was possible roughly to correlate the gross appearances of the various lesions in continuity with the subsequent grades of recovery. Four types of injury in continuity are distinguishable:

(i) The nerve looks and feels normal though there may be, perhaps, a little thickening of the sheath. The lesion will almost certainly be an axonotmesis and good spontaneous recovery will occur.

(ii) The nerve shows a smooth spindle-shaped swelling, the well-known fusiform neuroma. The damage is mainly interfascicular and here again spontaneous recovery is to be expected provided that the consistency of the nerve is not appreciably firmer than normal. If it is, further investigation is necessary and resection may be required.

(iii) The nerve is slightly narrowed or irregularly swollen, but the most striking feature is the palpable presence of scar tissue within its substance. Such a lesion requires investigation.

(iv) A lateral neuroma is present, which means that the nerve is partially divided. In these cases—but only where complete paralysis is present—there is always severe damage of the apparently healthy part of the nerve and resection and suture should be performed without hesitation.

Where there is palpable intraneural thickening, including the firm fusiform neuromata, trial incision is required. A transverse nick should be made in the nerve and deepened until bundles are exposed. This is a delicate operation, and it may be necessary to compress the nerve gently above and below in order to obtain a dry field. The incision should be started at the point where the thickening is greatest, and if more than half the nerve is found to be fibrotic, resection and suture should be performed. If these cases are left alone the results will be most disappointing.

If delay is so harmful, then what is the position as regards primary suture?

(4) *Unreliability of primary suture.*—Primary repair sometimes gives the most gratifying results, but I am now convinced that it is such an unpredictable operation that, except in the rare event of a nerve being cleanly divided accidentally during the course of an operation, it should not be performed. There are several reasons why the results are not uniformly satisfactory. The first and most important is that the agent severing the nerve often produces more or less severe interstitial damage in both stumps, which cannot be recognized at the time though it becomes manifest after three weeks as a zone of intraneural scarring. In one case the nerve showed dense collagenization at the site of suture over a length of 4 cm. An attempt to avoid this hazard by trimming of the stumps would involve quite arbitrary resection of both, and the result would be a gap that could only be closed by mobilization of the nerve stumps. Now although the risk of sepsis after simple closure of the primary wound may be remote, the addition of the long incision required for mobilization and the more or less intricate dissection that is called for would lead to disaster should sepsis supervene; mobilization, a very necessary step, is undesirable as a primary procedure. The nerve sheath, too, is in a poor state for taking sutures at the time of injury. Nowadays no one sutures a nerve; only the sheath is transfixed by the stitches and if it is frayed or split neat apposition is impossible. On the other hand, after three or four weeks the sheath in each stump often thickens in a most obliging fashion over a length of a centimetre or two and is in good condition for holding stitches. Lastly, the scar that is left after primary suture involves skin, subcutaneous tissues, the nerve itself, perhaps a few tendons and even the capsule of the subjacent joint. When movement is permitted the result is often a partial or complete separation of the suture line, the scar dragging on the nerve at its most vulnerable point; or there

(2) *Associated injuries* to blood-vessels, muscles, tendons and joints are a relatively unavoidable cause of failure. I say relatively because improvements in reconstructive surgery enable us to save limbs that only a few years ago would have been amputated. For example, one patient (*see Seddon, 1947b*) who lost almost every structure in the anterior compartment of the forearm yet has a useful hand as a result of a combination of plastic repair of the skin, arthrodesis of the wrist, nerve grafting and tendon transplantation.

(3) Some nerve lesions are too extensive to be repaired by any means now at our disposal, and in addition to the large traumatic gaps I include here cases in which the damage produced by traction extends over many inches, and those uncommon cases of ischaemic nerve injury in which a great length of nerve has become shrunken and fibrotic as a result of vascular damage. Yet even these cases may some day be tackled with success.

*Avoidable Causes of Failure* are much more numerous

(1) *A poor condition of the limb* must be mentioned first for it will preclude useful recovery even in those cases where it could occur spontaneously. Few situations are more depressing than that in which a favourable nerve injury is found in a limb that has been allowed to become stiff and wasted. The remedies, which call for the most devoted attention in their application, are fortunately well known; preservation of mobility, the limiting of splinting to what is essential for the prevention of overstretching of muscles and the control of atrophy by electrical stimulation.

(2) *Delay: when to explore.*—I need say no more about sepsis and the early repair of skin defects. But we now come to a major matter of policy; if delay is important, when should exploration be undertaken? Statistics from the United States, this country and Germany are consistent in showing that in cases where a nerve injury is due to an open wound there is a fifty-fifty chance of radical repair being needed.<sup>1</sup> There are only two ways of distinguishing these two groups—by exploration or by waiting to see what happens. If we wait, then in those cases where suture is necessary we shall have missed the opportunity of repairing the nerve at the most favourable time. I am sure, as are the Americans (Spurling, 1945; Spurling and Woodhall, 1946), that the correct policy is to explore at the earliest possible moment and to regard the operation, as Riddoch said so often, as an essential step in establishing the diagnosis. Nowadays it is safe to go in three weeks after healing of the wound. The situation is rather different in those cases where complete paralysis results from a closed fracture such as those of the humerus. In at least four out of five of these cases there is a favourable lesion in continuity, an axonotmesis, and excellent spontaneous recovery will occur. Conservative treatment is, therefore, appropriate in the first place, but should not be continued if paralysis persists beyond the time when evidence of recovery should be due. Here is a simple example (*Seddon, 1947a*). A fracture has occurred 12 cm. above the lateral epicondyle, and there is complete radial paralysis. The point of entry into brachioradialis of the motor branch of the radial nerve is about 2 cm. above the epicondyle. For practical purposes the rate of regeneration may be regarded as 1 mm. a day, and we should therefore expect a flicker of recovery in brachioradialis after about 100 days. It would be reasonable to wait 130 days, but not for longer; if at the end of this time there is still complete paralysis the nerve should be explored. In other situations the outlook is even more favourable, and I have never yet found it necessary to explore the nerves at the shoulder after closed fractures in that region.

(3) *Timidity in resecting lesions in continuity.*—In the early days of this work we were reluctant to resect nerves where, although complete paralysis was present, there

<sup>1</sup>Mr. Zachary tells me that the ratio of divisions to injuries in continuity was as high as 3 : 2 where paralysis was still complete when the patients reached a nerve injury centre.

TABLE VII. SUMMARY OF NERVE GRAFTS (1941-48)

|                               | Recovery | Partial recovery | Failure | Not traced | Total |
|-------------------------------|----------|------------------|---------|------------|-------|
| A. Digital .. ..              | 7        | 3                | 6       | —          | 16    |
| B. Cable:                     |          |                  |         |            |       |
| Median .. ..                  | 4        | 1                | 1       | —          | 7     |
| Brachial plexus ..            | —        | 1                | 3       | —          | 5     |
| Others .. ..                  | 3        | 2                | —       | —          | 5     |
| C. Main trunk:                |          |                  |         |            |       |
| Median .. ..                  | 9        | 2                | 2       | —          | 15    |
| Sciatic .. ..                 | —        | 3                | 5       | —          | 9     |
| Others .. ..                  | 1        | —                | 3       | —          | 4     |
| D. Inlay for partial division | 4        | 1                | 1       | 1          | 7     |
|                               | 28       | 8                | 21      | 1          | 68    |

resection of the stumps. There is little chance of error so far as the central stump is concerned for the very existence of a neuroma is an indication that it contains nerve fibres. However, if the ideal is to be attained, namely, the exposure of normal bundles, the site of section should not be distal to the neck of the neuroma. The peripheral stump presents a more difficult problem, for one occasionally finds serious collagenization involving bundles that appear normal to the naked eye; this collagenization is so dense as to present a complete barrier to the outgrowing axons. Fortunately this state of affairs is rare and seems to be associated with gross soft tissue damage and destruction of blood-vessels. It is almost certainly ischaemic in origin. In such a case the surgeon should be content not merely with exposing obvious bundles; he should try, if possible, to make his line of section distal to the zone of the original wound. In both stumps the sheath must be mobile, but an increase in interfascicular connective tissue can be ignored provided that the bundles stand out well from it when the nerve is gently squeezed. The state of the cut surfaces should be checked histologically.

(6) *Post-operative hazards.*—The first, sepsis, is now rare and I recall only one case in which separation of the stumps occurred. Superficial infection is unimportant but if deep infection occurs then it is probably wise to re-explore the nerve after an appropriate interval to find out what has happened at the suture line. A much more sinister hazard which, according to Spurling, occurs in 2.5% of cases, is separation of the stumps, and it is all the more disturbing since, unless some special technique is used, one has no warning of its occurrence. Spurling and his colleagues in the American Army used tantalum wire as suture material. They looked for post-operative separation of the stumps by radiography; and Spurling believed that some knots of wire always went with one stump and the rest with the other. Yet this may not be invariable and the only wholly reliable kind of marker is one that is attached to the stump itself, away from the suture line, and for this reason I have used either small loops of wire or gold plates attached to the epineurium 2 or 3 mm. away from the line of suture. A curious feature of this separation is that, in our experience, it always occurs before there has been any post-operative stretching. It may be that the suture line is burst asunder by a haematoma from an oozing vessel in one nerve stump; it is also possible, though so far we have obtained no proof of it, that collagen formation is defective on account of a subcorbutic state. The plates are used only in situations where the post-operative stretching will fall chiefly on the suture line; a radiograph is taken at the time when the first plaster is changed three weeks after operation and again when stretching has been completed.

#### CONCLUSION

Hitherto, peace-time peripheral nerve surgery has suffered from being nobody's business. Yet the penalty for failure is a heavy one. And now that it seems clear

may be permanent restriction of movement from adhesion of the nerve to the surrounding structures. Zachary and Holmes (1946) have compared the results in 55 cases of primary suture with those after early secondary suture and there is no question that the latter are far superior. It happens that in a series of 31 cases of nerve injury at the wrist treated by secondary suture there has not been a single failure, and I think that if early secondary suture is performed, with adequate mobilization, a useful result can almost be guaranteed. This condemnation of primary suture has met with some opposition, but I am not aware that anyone else has compared the results of the primary operation with early secondary repair, and primary suture can be justified only on such a basis.

The correct technique for a clean wound at the wrist is to tack the nerve ends together with as little rotation as possible, to close the skin wound and to re-explore through a comfortable and adequate incision, three or four weeks later, when all induration has subsided and the soft tissues are mobile.

The most important and serious peace-time nerve injuries are the comparatively clean wounds at the wrist, and concomitant severance of a few or many tendons is fairly frequent. The aim should be to perform a primary suture of the tendons, to tack the nerve ends together and to close the skin. Formal nerve suture should be postponed until restoration of tendon function is well advanced. The scar of the original wound is then excised, a small incision is carried distally and a long one proximally, the central stump is freely mobilized, and suture is performed not merely in a position that permits easy apposition of the resected stumps but in one that permits normal activity in the long flexors of the wrist and digits. Thus, it may even be desirable to suture the nerves with the wrist in slight dorsiflexion, which presents no difficulty—though the operation is a tedious one—if mobilization is carried as far proximally as the lower quarter of the arm, the nerve ends being brought together with the elbow flexed to a right-angle.

(5) *Errors in the technique of secondary suture.*—Inadequate mobilization. The aim must be to mobilize the stumps so extensively that they come together with ease, the stitches being required merely to ensure closure of the epineurium. Many poor results after nerve suture at the wrist are due to failure to mobilize the median or ulnar nerve as far proximally as the upper third of the forearm or even up to the lower third of the arm. I found that one or other of these procedures was necessary in 26 out of 31 cases (Table VI). To suture either nerve with the wrist flexed more than 45 degrees is

TABLE VI.—MOBILIZATION REQUIRED FOR NERVE INJURIES AT THE WRIST

| Extent                          | Number of cases | Gaps to be closed |
|---------------------------------|-----------------|-------------------|
| To lower third of arm .. ..     | 15              | 2.5-7 cm.         |
| To upper third of forearm .. .. | 11              | 1.5-5 cm.         |
| To lower third of forearm .. .. | 5               | up to 3 cm.       |

to invite risk of partial separation when the joint is mobilized. The same is true of the posterior tibial nerve at the ankle.

The converse error, that has already been mentioned, is the closure of very large gaps by extensive mobilization and suture of the nerve with a joint in an acutely flexed position. Table V shows the critical resection lengths for all the important nerves. But good recovery is only possible, not certain, in cases where there are these quite considerable gaps. So these figures should be taken as maximal rather than optimal, and where circumstances permit the employment of an autogenous graft it may be wise to choose this alternative even though a gap may not exceed a figure shown in this table. The results of grafting are summarized in Table VII and I have given an account of them elsewhere (Seddon, 1947b).

An otherwise satisfactory operation may be marred or even ruined by inadequate

TABLE VII. AUTOGENOUS NERVE GRAFTS  
SUMMARY OF RESULTS (1941-48)

|                               |    |    | Recovery | Recovering | Partial recovery | Failure | Not traced | Total |
|-------------------------------|----|----|----------|------------|------------------|---------|------------|-------|
| A. Digital                    | .. | .. | 7        |            | 3                | 6       | —          | 16    |
| B. Cable:                     |    |    |          |            |                  |         |            |       |
| Median                        | .. | .. | 4        |            | 2                | 1       | —          | 7     |
| Brachial plexus               | .. | .. | —        | 1          | 1                | 3       | —          | 5     |
| Others                        | .. | .. | 3        |            | 2                | —       | —          | 5     |
| C. Main trunk:                |    |    |          |            |                  |         |            |       |
| Median                        | .. | .. | 9        | 2          | 2                | 2       | —          | 15    |
| Sciatic                       | .. | .. | —        | 1          | 3                | 5       | —          | 9     |
| Others                        | .. | .. | 1        |            | —                | 3       | —          | 4     |
| D. Inlay for partial division |    |    | 4        | 1          | —                | 1       | 1          | 7     |
|                               |    |    | 28       | 5          | 13               | 21      | 1          | 68    |

resection of the stumps. There is little chance of error so far as the central stump is concerned for the very existence of a neuroma is an indication that it contains nerve fibres. However, if the ideal is to be attained, namely, the exposure of normal bundles, the site of section should not be distal to the neck of the neuroma. The peripheral stump presents a more difficult problem, for one occasionally finds serious collagenization involving bundles that appear normal to the naked eye; this collagenization is so dense as to present a complete barrier to the outgrowing axons. Fortunately this state of affairs is rare and seems to be associated with gross soft tissue damage and destruction of blood-vessels. It is almost certainly ischaemic in origin. In such a case the surgeon should be content not merely with exposing obvious bundles; he should try, if possible, to make his line of section distal to the zone of the original wound. In both stumps the sheath must be mobile, but an increase in interfascicular connective tissue can be ignored provided that the bundles stand out well from it when the nerve is gently squeezed. The state of the cut surfaces should be checked histologically.

(6) *Post-operative hazards.*—The first, sepsis, is now rare and I recall only one case in which separation of the stumps occurred. Superficial infection is unimportant but if deep infection occurs then it is probably wise to re-explore the nerve after an appropriate interval to find out what has happened at the suture line. A much more sinister hazard which, according to Spurling, occurs in 2.5% of cases, is separation of the stumps, and it is all the more disturbing since, unless some special technique is used, one has no warning of its occurrence. Spurling and his colleagues in the American Army used tantalum wire as suture material. They looked for post-operative separation of the stumps by radiography; and Spurling believed that some knots of wire always went with one stump and the rest with the other. Yet this may not be invariable and the only wholly reliable kind of marker is one that is attached to the stump itself, away from the suture line, and for this reason I have used either small loops of wire or gold plates attached to the epineurium 2 or 3 mm. away from the line of suture. A curious feature of this separation is that, in our experience, it always occurs before there has been any post-operative stretching. It may be that the suture line is burst asunder by a haematoma from an oozing vessel in one nerve stump; it is also possible, though so far we have obtained no proof of it, that collagen formation is defective on account of a subscorbatic state. The plates are used only in situations where the post-operative stretching will fall chiefly on the suture line; a radiograph is taken at the time when the first plaster is changed three weeks after operation and again when stretching has been completed.

#### CONCLUSION

Hitherto, peace-time peripheral nerve surgery has suffered from being nobody's business. Yet the penalty for failure is a heavy one. And that it seems clear

may be permanent restriction of movement from adhesion of the nerve to the surrounding structures. Zachary and Holmes (1946) have compared the results in 55 cases of primary suture with those after early secondary suture and there is no question that the latter are far superior. It happens that in a series of 31 cases of nerve injury at the wrist treated by secondary suture there has not been a single failure, and I think that if early secondary suture is performed, with adequate mobilization, a useful result can almost be guaranteed. This condemnation of primary suture has met with some opposition, but I am not aware that anyone else has compared the results of the primary operation with early secondary repair, and primary suture can be justified only on such a basis.

The correct technique for a clean wound at the wrist is to tack the nerve ends together with as little rotation as possible, to close the skin wound and to re-explore through a comfortable and adequate incision, three or four weeks later, when all induration has subsided and the soft tissues are mobile.

The most important and serious peace-time nerve injuries are the comparatively clean wounds at the wrist, and concomitant severance of a few or many tendons is fairly frequent. The aim should be to perform a primary suture of the tendons, to tack the nerve ends together and to close the skin. Formal nerve suture should be postponed until restoration of tendon function is well advanced. The scar of the original wound is then excised, a small incision is carried distally and a long one proximally, the central stump is freely mobilized, and suture is performed not merely in a position that permits easy apposition of the resected stumps but in one that permits normal activity in the long flexors of the wrist and digits. Thus, it may even be desirable to suture the nerves with the wrist in slight dorsiflexion, which presents no difficulty—though the operation is a tedious one—if mobilization is carried as far proximally as the lower quarter of the arm, the nerve ends being brought together with the elbow flexed to a right-angle.

(5) *Errors in the technique of secondary suture.*—Inadequate mobilization. The aim must be to mobilize the stumps so extensively that they come together with ease, the stitches being required merely to ensure closure of the epineurium. Many poor results after nerve suture at the wrist are due to failure to mobilize the median or ulnar nerve as far proximally as the upper third of the forearm or even up to the lower third of the arm. I found that one or other of these procedures was necessary in 26 out of 31 cases (Table VI). To suture either nerve with the wrist flexed more than 45 degrees is

TABLE VI.—MOBILIZATION REQUIRED FOR NERVE INJURIES AT THE WRIST

| Extent                       | Number of cases | Gaps to be closed |
|------------------------------|-----------------|-------------------|
| To lower third of arm .. ..  | 15              | 2.5-7 cm.         |
| To upper third of forearm .. | 11              | 1.5-5 cm.         |
| To lower third of forearm .. | 5               | up to 3 cm.       |

to invite risk of partial separation when the joint is mobilized. The same is true of the posterior tibial nerve at the ankle.

The converse error, that has already been mentioned, is the closure of very large gaps by extensive mobilization and suture of the nerve with a joint in an acutely flexed position. Table V shows the critical resection lengths for all the important nerves. But good recovery is only possible, not certain, in cases where there are these quite considerable gaps. So these figures should be taken as maximal rather than optimal, and where circumstances permit the employment of an autogenous graft it may be wise to choose this alternative even though a gap may not exceed a figure shown in this table. The results of grafting are summarized in Table VII and I have given an account of them elsewhere (Seddon, 1947b).

An otherwise satisfactory operation may be marred or even ruined by inadequate

## Section of Surgery

President—JULIAN TAYLOR, C.B.E., M.S., F.R.C.S.

[January 5 1949]

The following specimens were shown:

(1) Unusually Large Diverticulum of the Bladder. (2) Large Calcified Tumour or Cyst of the Kidney for Diagnosis. (3) Carcinoma of the Duodenum. (4) Primary Carcinoma of the Ileum.—Professor C. A. WELLS.

Pedunculated Carcinoma of the Œsophagus.—Mr. RODNEY SMITH.

(1) Peri-renal Fibrosarcoma. (2) Congenital Diverticulum of the Bladder. (3) Bleeding Peptic Ulcer in Meckel's Diverticulum (Diagnosed in a Child of 8 months).—Mr. ANTHONY S. TILL.

Reconstructive Endo-aneurysmorrhaphy with Vein-graft Inlay.—Mr. ALAN H. HUNT.

Carcinoma of the Ampulla of Vater.—Mr. R. S. HANDLEY.

(1) Congenital Duplication of the Gall-bladder with Cholesterosis on One Side. (2) Traumatic Aneurysms. (3) Advanced Carcinoma of the Rectum Treated by Wertheim's Hysterectomy and Resection of the Rectum and Lower Sigmoid Colon.—Mr. M. C. OLDFIELD.

Carcinoma of the Cæcum Fungating Through a Recent Appendicectomy Incision.—Mr. J. SCHOLEFIELD.

Paraplegia Resulting from Diffuse Bony Compression of Unknown Pathology. ? Osteitis Fibrosa. ? Melorheostosis.—Mr. C. P. SAMES.

Fibrosarcoma of Breast Arising in a Fibro-adenoma of Pericanalicular Type.—Mr. WALLACE BLACK.

(1) Congenital Non-Meckelian Diverticulum of Ileum. (2) Diverticulosis of the Appendix.—Mr. B. N. BROOKE.

Chronic Ileitis.—Mr. E. P. HALL DRAKE.

[March 2, 1949]

## DISCUSSION ON THE SURGERY OF PORTAL HYPERTENSION

Professor Sir James Learmonth:

ABSTRACT.—In the surgical treatment of portal hypertension, three problems present: (1) mesenteric venous thrombosis, (2) hæmorrhage from the alimentary tract, and (3) ascites.

Attempts to reduce the risk of hæmorrhage—which generally arises from œsophageal varices—have been made by the following procedures: (1) splenectomy; (2) ligation of the splenic artery; (3) omentopexy; (4) ligation of the left gastric veins; (5) ligation of all peri-œsophageal veins; (6) injection of œsophageal varices; and (7) portal-caval shunts. In 13 personal cases, portal-caval shunt has been carried out by means of end-to-end spleno-renal anastomosis after splenectomy and left nephrectomy. Five of these patients died after operation. The finding at autopsy, in one of these fatalities, of the formation of a natural portal-caval shunt, which had not prevented œsophageal bleeding, raised a doubt as to the efficacy of an artificial shunt to reduce portal hypertension. Although hæmatemesis has occurred in one of the surviving patients, their general health has been excellent, except for one patient in whom ascites persisted.

Six children have undergone splenectomy for hæmatemesis due to splenic thrombosis. One patient died twenty-three months after operation as a result of a massive hæmorrhage from an œsophageal varix. At autopsy, although pathological signs of severe portal hypertension were found in the portal vein, there was absence of any effort at the formation of a collateral circulation and of any histological evidence of damage to liver cells.



that primary repair is not merely devoid of special merit, but actually undesirable, patients with nerve injuries can always be dealt with at leisure and with the degree of technical skill which in the past they have too often been denied.

A more detailed account of peripheral nerve surgery will be found in the author's review in War Surgery Supplement No. 2. *British Journal of Surgery*, Wounds of the Extremities, January, 1949.

#### REFERENCES

- ABERCROMBIE, M., and JOHNSON, M. L. (1942) *J. exp. Biol.*, 19, 266.  
BALLANCE, C., and DUEL, A. M. (1932) *Arch. Otolaryng.*, 15, 1.  
BOWDEN, R. E. M., and GUTMANN, E. (1944) *Brain*, 67, 273.  
BROOKS, D. M. (1949) *J. Bone Jt. Surg.*, 31B, 17.  
BUNNELL, STERLING (1927) *Surg. Gynec. Obstet.*, 44, 145.  
——, and BOYES, J. A. (1939) *Amer. J. Surg.*, 44, 64.  
DAVIS, D. R. (1949) *Lancet*, (i), 877.  
GUTMANN, E., and YOUNG, J. Z. (1944) *J. Anat. Lond.*, 78, 15.  
HIGHT, W. B., and HOLMES, W. (1943) *Brit. J. Surg.*, 30, 212.  
——, and SANDERS, F. K. (1943) *Brit. J. Surg.*, 30, 355.  
HOLMES, W., and YOUNG, J. Z. (1942) *J. Anat. Lond.*, 77, 63.  
JACKSON, E. C. S. (1945) *Brain*, 68, 300.  
——, and SEDDON, H. J. (1945) *Brit. med. J.* (ii), 485.  
SEDDON, H. J. (1947a) *J. Amer. med. Ass.*, 135, 691.  
—— (1947b) *Brit. J. Surg.*, 35, 151.  
SPURLING, R. G. (1945) *J. Amer. med. Ass.*, 129, 1011.  
——, and WOODHALL, B. (1946) *Ann. Surg.*, 123, 731.  
STOPFORD, J. S. B. (1920a) *Proc. R. Soc. Med.*, 13, 67.  
—— (1920b) *Brain*, 43, 1.  
ZACHARY, R. B., and HOLMES, W. (1946) *Surg. Gynec. Obstet.*, 82, 632.

The point at issue is whether the hypertension. The problems with which venous thrombosis, (2) hæmorrhage, and (3) ascites. I propose to deal mainly with hæmorrhage.

#### *Hæmorrhage.*

In the majority of cases the source of the collateral circulation develops from the portal vein, or when blood from the portal vein is prevented from being distributed through the gastric vein of the portal system. Less frequently the source is the stomach. In patients suffering from portal hypertension, the appearance of œsophageal varices is a direct or contributory cause of death. These are vulnerable veins, long before reduction of the pressure in the portal system. In cirrhosis, 50% die within a year of the first hæmorrhage. It is not a matter for surprise that surgical efforts have been made to reduce the risk of massive bleeding from œsophageal varices:

(1) *Splenectomy* alone is said to reduce the amount of blood reaching the portal vein by about 40%. Division of the vasa brevia is said to reduce the amount of blood reaching the varices, but obviously may not reduce the pressure within them if they are still open to reflux from the left gastric veins. Splenectomy does not influence the occurrence of hæmatemesis (Howells, 1938).

(2) *Ligation of the splenic artery* reduces the amount of blood reaching the spleen and ultimately the portal vein, while leaving intact the venous collaterals connected with the organ. It is an attractive idea (McNee, 1931), of which I have little experience; and it does not seem to have been generally used.

(3) *Omentopexy*, in its many forms, seeks to encourage the formation of communications between portal and systemic systems; it may hasten the development of an adequate collateral circulation in cases where in any event the latter would be adequate.

(4) *Ligation of the left gastric veins* deals with only one set of feeders, but

(5) *Ligation of all peri-œsophageal veins*, with or without *œsophagogastrrectomy*, seeks to remove both feeders and danger point.

(6) *Injection of œsophageal varices* in order to produce thromboses within them is open to the same objection as is the injection of varicose veins of the leg, in the presence of an incompetent saphenous vein.

In 1945 surgeons were glad to welcome the brilliant work of Whipple (1945) and of Blakemore and Lord (1945), who suggested that

(7) *Portal-caval shunts* might provide the solution of the problem, by depleting the portal system and reducing the pressure in it. The original shunts suggested were (a) portal vein—superior vena cava end-to-side, and (b) splenic vein—left renal vein end-to-end; others have been employed since (Linton, 1948), (c) splenic vein—left renal vein end-to-side, (d) superior mesenteric vein—superior vena cava end-to-side, and (e) inferior mesenteric vein—left ovarian vein end-to-side.

In 1940 I made an Eck fistula by the cutting ligature method in a case of hepato-lienal fibrosis, but the patient died of bronchopneumonia on the sixth day and at autopsy the anastomosis was found occluded by clot. Since Whipple's publication I have constructed a portal-caval shunt on 13 occasions, of which 11 were made with the aid of a Blakemore vitallium tube, and two were direct anastomoses. All have been end-to-end splenic vein—left renal vein anastomoses, after splenectomy and left nephrectomy. Apart from the technical difficulty of isolating the portal vein from a tangle of collaterals, animals in which an Eck fistula has been constructed deteriorate so progressively that I have wondered whether it is a desirable procedure in man. I have used end-to-end spleno-renal anastomosis because on engineering grounds a conduit will operate most effectively if it is not asked to accept much more than its normal load. I do not think that the so-called sucking action of the blood in the renal vein can be more effectual in draining the portal system of blood, than are the low pressures in the inferior vena cava, together with its respiratory changes in length and calibre. End-to-side anastomoses operate better when the vessels are so situated that the arriving blood enters in the same direction as the receiving blood is flowing; this is the general arrangement in the body.

In 5 cases, after splenectomy I have abandoned the attempt to construct a spleno-renal anastomosis, because of the absence of any branch of the splenic vein of sufficient size to make a shunt worth while.

part in the treatment of portal hypertension may be posed by (1) mesenteric thrombosis, (2) hæmorrhage from the rectum, and (3) ascites. I propose

to deal with the œsophageal varices, forming part of the collateral circulation. If blood from the spleen fails to reach the liver, it is prevented from reaching the liver or the portal vein by the link up the vasa brevia and the left gastric vein. The hemiazygos veins of the systemic circulation and a varicose vein in the fundus of the stomach, or from hepato-lienal fibrosis, the blood from these anatomically exceedingly vulnerable veins is a threat to life; in cases of hæmorrhage. It is not a matter for surprise that surgical efforts have been made to reduce the risk of massive bleeding from œsophageal varices:

RÉSUMÉ.—Trois problèmes se présentent dans le traitement de l'hypertension portale: (1) le thrombose veineuses mésentériques, (2) les hémorragies des voies alimentaires et (3) les ascites.

Les procédés suivants ont été essayés pour combattre le risque des hémorragies, qui proviennent le plus souvent de varices oesophagiennes: (1) la splénectomie, (2) la ligature de l'artère splénique, (3) l'omentopexie, (4) la ligature des veines gastriques gauches, (5) la ligature de toutes les veines péri-oesophagiennes, (6) l'injection des varices oesophagiennes, (7) la dérivation porto-cavale. Ce dernier procédé a été employé par l'auteur chez 13 malades au moyen d'une anastomose spléno-rénale termino-terminale, après splénectomie et néphrectomie gauche. Cinq sont morts après l'opération. L'autopsie dans un de ces cas a révélé une dérivation porto-cavale spontanée qui n'avait pas empêché l'hémorragie oesophagienne, ce qui fait surgir des doutes de l'efficacité d'une dérivation artificielle pour la réduction de l'hypertension portale. Quoique l'hématémèse ait récidivé chez un des survivants, leur état général est excellent, sauf dans un cas où l'ascite persiste.

Six enfants ont été splénectomisés pour hématémèse par thrombose splénique. L'un d'eux est mort après 23 mois à la suite d'une hémorragie massive d'une varice oesophagienne. Malgré la présence d'une hypertension portale grave l'autopsie n'a révélé aucune tendance à la formation d'une circulation collatérale, ni aucune lésion des cellules hépatiques.

КОНСИЕКТ.—Хирургия при увеличении кровяного давления в воротной вене представляет три проблемы: 1/ брижеечный венозный тромбоз; 2/ кровотечение из пищеварительного тракта; 3/ водянка живота.

Для уменьшения риска кровотечения, которое обыкновенно происходит из варикозных узлов пищевода, были испробованы следующие операции: 1/ удаление селезенки; 2/ перевязка селезеночной артерии; 3/ саллингопексия; 4/ перевязка левых вен желудка; 5/ перевязка всех пери-пищеводных вен; 6/ вырезывания в парикозные узлы пищевода; и 7/ перемычка между воротной и нижней поллой венами (vena porta и vena cava). В 13-ти случаях, произведенных лично, перемычка между воротной и нижней поллой венами была сделана путем селезеночного-почечного анастомоза/конец с концом/ после удаления селезенки и левой почки. Пять из этих больных умерли после операции. При вскрытии одного из этих пяти было найдено, что образование естественного анастомоза между воротной и нижней поллой венами не предотвратило кровотечения из пищевода, и оттого польза искусственного анастомоза для уменьшения кровяного давления в воротной вене является сомнительной. Хотя кровотечение из желудка и повторилось у одного из выживших больных, их общее состояние было превосходно, за исключением одного больного, у которого водянка живота не уменьшилась.

Шестерым детям было сделано удаление селезенки по поводу кровяной рвоты вследствие селезеночного тромбоза. Один больной умер 23 месяца после операции вследствие сильного кровотечения из варикозного узла пищевода. Хотя при вскрытии и были найдены патологические явления высокого кровяного давления в воротной вене, было полное отсутствие попытки организма образования побочного кровообращения, а также отсутствие повреждения печеночных клеток с гистологической точки зрения.

RESUMEN.—En el tratamiento de la hipertensión portal, se presentan tres problemas: (1) la trombosis mesentérica venosa, (2) la hemorragia del canal alimenticio y (3) la ascitis.

Para reducir el peligro de hemorragia, que generalmente surge de las varices esofágicas varios intentos se han llevado a cabo por medio de los siguientes procedimientos: (1) la esplenotomía; (2) la ligadura de la arteria esplénica; (3) la omentopexia; (4) la ligadura de las venas gástricas del lado izquierdo; (5) la ligadura de todas las venas periesofágicas; (6) la inyección de las varices esofágicas y (7) las desviaciones porta-cavales. En 13 casos de observación personal la desviación porta-caval se ha llevado a cabo por medio de una anastomosis bazo renal de cabo a cabo después de la esplenotomía y nefrectomía del lado izquierdo. Cinco de estos pacientes fallecieron después de la operación. El hecho de haberse encontrado durante la autopsia en uno de los fallecidos la formación natural de una desviación porta-caval, que no había evitado el derrame sanguíneo esofágico, dio origen a que se dudara de la eficacia de la desviación artificial para reducir la hipertensión portal. A pesar de que la hematemesis ha reaparecido en uno de los pacientes que sobrevivieron, el estado general de su salud era excelente con la excepción de uno de ellos en el cual persistió la ascitis.

Debido a la hematemesis causada por la trombosis esplénica en seis niños se llevo a cabo la esplenotomía. Uno de los pacientes falleció 23 meses después de la operación a consecuencia de una gran hemorragia de una variz esofágica. En la autopsia a pesar de que se habían encontrado síntomas patológicos de una grave hipertensión portal en la vena porta no había signo alguno que indicara una tendencia hacia la formación de una circulación colateral así como tampoco ninguna evidencia histológica de que las células del hígado hubiesen sufrido daño alguno.

## RESULTS

Of the 8 patients who have survived the operation of spleno-renal anastomosis, one has been observed for only one month. Of the remaining 7, 4 were operated upon for hæmatemesis. Of these 4, 3 have had no recurrence of bleeding after periods ranging from twenty-four to thirty-two months; the fourth has had three large hæmatemeses, twelve months after operation. 2 patients had both ascites and hæmatemesis. One of them remains free from both after twenty-two months, the other has no further bleeding after eight months, but the ascites has persisted, although within the last month reaccumulation of fluid has been less rapid.

An aspect of the subject which has been of great interest to me has been the excellent health enjoyed by these patients since operation, with the one exception of the patient in whom ascites persisted. All feel well, all have put on weight, and 5 of them lead active lives; 2 play games. I have been unable to correlate this general well-being with improvement in hepatic function.

I have operated for hæmatemesis on 6 children, who have had histories of episodes of hæmatemesis, in 1 case beginning shortly after birth, and usually separated by intervals measured in years. In all these cases the liver was normal, and the distribution of collateral vessels was apparently limited to the vasa brevia system. I thought the diagnosis of thrombosis affecting the splenic vein fairly certain, and omitted to make observations on the relative pressures in the splenic vein, and in other branches of the portal system, or to make portal pyelograms; an omission which I regret.

One has been operated on for only a month. 3 children have had no further bleeding, after intervals of twenty-four, twelve and four months respectively. One has had a recurrence of hæmatemesis after seven months, and one died of a massive hæmorrhage after leading an active life for twenty-three months. The findings at autopsy in this last case were so unexpected that I am now dissatisfied with my diagnosis and treatment of the others.

The source of the bleeding was a varix in the œsophagus. The only evidence of collateral channels between portal and systemic circulations was between the capsule of the liver and the under surface of the diaphragm. The liver was normal in size and shape, its capsule was smooth, and its cut surface presented no macroscopic evidence of fibrosis or of disturbance of lobular pattern, and it was normal microscopically. When a cut was made across the porta hepatis, the portal vein was found to disappear into a mass of cavernomatous tissue. The middle coat of the portal vein was greatly hypertrophied; but the most surprising finding in its extrahepatic course was several calcareous plaques, over one of which an atheromatous ulcer had formed. I cannot explain the presence in the vein of these pathological signs of severe portal hypertension, and the absence of any effort at the formation of a collateral circulation and of any histological evidence of damage to liver cells.

In a similar case, operated on last week, I thought I could detect early signs of the formation of a collateral circulation in the round ligament and gastro-hepatic omentum. I exposed the splenic pedicle through the gastro-splenic omentum, and found a large splenic vein. Splenic pyelography was inconclusive. I thought it best to divide the splenic artery between ligatures, in the hope that the resulting reduction in input would tide the child over a period. If hæmatemesis recurs, I hope I shall have something better to offer: if I have not, at least the anastomosis will be more easily fashioned.

I am greatly indebted to my colleagues in Edinburgh and elsewhere who entrusted these patients to my care.

## REFERENCES

- BLAKEMORE, A. H., and LORD, J. W., Jr. (1945) *Ann. Surg.*, 122, 476.  
 HAGELSTAM, L. (1944) *Acta Chir. Scand.*, 90, 37.  
 HOWELLS, N. (1938) *Lancet* (i), 1320.  
 LINTON, R. R. (1948) *New Engl. J. Med.*, 238, 723.  
 MCNEE, J. W. (1931) *Lancet* (i), 951, 1009, 1063.  
 WHIPPLE, A. O. (1945) *Ann. Surg.*, 122, 449.

Professor R. Milnes Walker:

**ABSTRACT.**—Portal obstruction may be intrahepatic or extrahepatic; in the latter case it is important to recognize the site; the diagnosis can best be confirmed by the demonstration of œsophageal varices, either by radiography or œsophagoscopy.

Estimation of the serum albumin gives the best indication of the state of liver function, and a level below 2.5 mg. % indicates that it is gravely impaired. Portal pressures up to 450 mm. of water have been found in the cases reported. A transverse upper abdominal incision gives good access and can be enlarged to the right for exposure of the portal vein, or to the left if a lieno-renal venous anastomosis is to be performed. As removal of the spleen entails removal of some of the collateral circulation, anastomosis between the portal vein and inferior vena cava is to be preferred when this is possible, but engorged veins around the portal vein may render this procedure impractical.

One case was subjected to laparotomy only, and in another (kindly referred to me by Professor Charles Wells), a child who had previously undergone splenectomy, I was unable to construct any form of anastomosis.

The clinical diagnosis in these 13 cases was :

|                                       |          |
|---------------------------------------|----------|
| Hepato-lienal fibrosis .. .. .        | 4        |
| Hepatitis with { Balloon dope .. .. . | 1        |
| { ? Alcoholic .. .. .                 | 1        |
| { Infective .. .. .                   | 3        |
| Hepatic cirrhosis .. .. .             | 4        |
|                                       | <hr/> 13 |

Of these 13 patients, 5 died after the operation.

(1) F., aged 46, a case of hepato-lienal fibrosis, died twelve hours after operation, without regaining consciousness. An autopsy was not done, and except for the observation that the clinical picture was not that of shock, I cannot explain this death. Professor Charles Wells has told me of a patient of his who remained unconscious for twenty-four hours, and then recovered.

(2) M., aged 48, a case of hepatic cirrhosis with a history of alcoholism. This patient died of pulmonary œdema, thirty-two hours after operation. In spite of a failing circulation, the anastomosis was patent.

(3) M., aged 24, a case of hepato-lienal fibrosis. This patient was the only one in whom a combined thoraco-abdominal approach was used. Though this gave excellent access, and the operation site appeared dry at the conclusion of the procedure, the cause of death five days after operation was hæmorrhage from the operation site, and into the alimentary tract. The anastomosis was twisted but still patent: it had been made by direct end-to-end suture.

(4) M., aged 19, a case of advanced hepatic cirrhosis, died six days after operation. For four days he did very well, then had a hæmatemesis, became confused, and developed a left hemiplegia. As this was thought to be due to cerebral thrombosis, heparin was given. Pulse-rate and blood-pressure rose gradually, the confusion deepened to coma, but there was no further hæmatemesis.

At autopsy the stomach and intestine were found full of blood, and the anastomosis was blocked by a thrombus. The bleeding had occurred from varicosities in the fundus of the stomach, and was naturally increased by heparinization. Probably it began after the anastomosis became occluded. The brain and its vessels were normal, and the neurological signs must have been due to cerebral ischæmia.

I shall deal with the extent of thrombosis at the anastomosis after the next case.

(5) M., aged 44, a case of advanced hepatic cirrhosis, died four days after operation, the clinical features in this period being oliguria, increasing icterus, and increasing coma; there was massive terminal bleeding into the stomach from œsophageal varices. The portal vein was blocked by a thrombus, partly old, largely recent, which extended into the splenic vein but did not occlude the anastomosis.

When the anastomosis in Case 4, together with the splenic and renal veins, was examined, it was found that the thrombus appeared to be limited to the parts of the veins distal to the points of application of the temporary bulldog clamps, and it may be that the period of ischæmia of the walls of the veins, while they were being prepared for the anastomosis, led to intimal damage which induced clotting. I think it would be best to free both splenic and renal veins, and to clamp their ends with ordinary artery forceps, leaving the stumps full of blood until the last moment before the anastomosis.

The specimen also showed a feature which gives food for thought. The usual origin of the hemiazygos vein is the left lumbar azygos vein, arising from the posterior aspect of the left renal vein. It is known that in many cases of portal obstruction, one of the collateral routes from the splenic vein, or from diaphragmatic collaterals, is to the left adrenal vein and thence to the left renal vein, and that occasionally a direct collateral from the splenic vein joins the renal vein. In this particular specimen a large vein, of an internal diameter of 6 mm., joined the upper border of the left renal vein. This is a natural portal-caval shunt, and it is as large as can usually be constructed by the surgeon. Its failure to prevent œsophageal bleeding in this patient makes one wonder if limited shunting is really an effective way of trying to reduce portal hypertension. The adrenal and lumbar veins are often more numerous than what is somewhat arbitrarily regarded as normal, and, when this is so, a patient suffering from portal hypertension may be less liable to bleed from œsophageal varices.

It is interesting to examine Linton's figures for portal pressures before and after shunts: in two cases the pressure was not reduced after the shunt, and in one case the pre-operative pressure was actually lower than that after the shunt in other cases.

It has been pointed out (Hagelstam, 1944) that the damaged liver has a diminished capacity to remove citric acid from the blood. It may be that the large amounts of citrated blood used in the attempt to resuscitate patients who bleed after operation may actually encourage bleeding by adding enough citrate to the circulating blood to make it incoagulable.

## RESULTS

Of the 8 patients who have survived the operation of spleno-renal anastomosis, one has been observed for only one month. Of the remaining 7, 4 were operated upon for hæmatemesis. Of these 4, 3 have had no recurrence of bleeding after periods ranging from twenty-four to thirty-two months; the fourth has had three large hæmatemeses, twelve months after operation. 2 patients had both ascites and hæmatemesis. One of them remains free from both after twenty-two months, the other has no further bleeding after eight months, but the ascites has persisted, although within the last month reaccumulation of fluid has been less rapid.

An aspect of the subject which has been of great interest to me has been the excellent health enjoyed by these patients since operation, with the one exception of the patient in whom ascites persisted. All feel well, all have put on weight, and 5 of them lead active lives; 2 play games. I have been unable to correlate this general well-being with improvement in hepatic function.

I have operated for hæmatemesis on 6 children, who have had histories of episodes of hæmatemesis, in 1 case beginning shortly after birth, and usually separated by intervals measured in years. In all these cases the liver was normal, and the distribution of collateral vessels was apparently limited to the vasa brevia system. I thought the diagnosis of thrombosis affecting the splenic vein fairly certain, and omitted to make observations on the relative pressures in the splenic vein, and in other branches of the portal system, or to make portal pyelograms; an omission which I regret.

One has been operated on for only a month. 3 children have had no further bleeding, after intervals of twenty-four, twelve and four months respectively. One has had a recurrence of hæmatemesis after seven months, and one died of a massive hæmorrhage after leading an active life for twenty-three months. The findings at autopsy in this last case were so unexpected that I am now dissatisfied with my diagnosis and treatment of the others.

The source of the bleeding was a varix in the œsophagus. The only evidence of collateral channels between portal and systemic circulations was between the capsule of the liver and the under surface of the diaphragm. The liver was normal in size and shape, its capsule was smooth, and its cut surface presented no macroscopic evidence of fibrosis or of disturbance of lobular pattern, and it was normal microscopically. When a cut was made across the porta hepatis, the portal vein was found to disappear into a mass of cavernomatous tissue. The middle coat of the portal vein was greatly hypertrophied; but the most surprising finding in its extrahepatic course was several calcareous plaques, over one of which an atheromatous ulcer had formed. I cannot explain the presence in the vein of these pathological signs of severe portal hypertension, and the absence of any effort at the formation of a collateral circulation and of any histological evidence of damage to liver cells.

In a similar case, operated on last week, I thought I could detect early signs of the formation of a collateral circulation in the round ligament and gastro-hepatic omentum. I exposed the splenic pedicle through the gastro-splenic omentum, and found a large splenic vein. Splenic pyelography was inconclusive. I thought it best to divide the splenic artery between ligatures, in the hope that the resulting reduction in input would tide the child over a period. If hæmatemesis recurs, I hope I shall have something better to offer: if I have not, at least the anastomosis will be more easily fashioned.

I am greatly indebted to my colleagues in Edinburgh and elsewhere who entrusted these patients to my care.

## REFERENCES

- BLAKEMORE, A. H., and LORD, J. W., Jr. (1945) *Ann. Surg.*, 122, 476.  
 HAGELSTAM, L. (1944) *Acta Chir. Scand.*, 90, 37.  
 HOWELLS, N. (1938) *Lancet* (i), 1320.  
 LINTON, R. R. (1948) *New Engl. J. Med.*, 238, 723.  
 MCNEE, J. W. (1931) *Lancet* (i), 951, 1009, 1063.  
 WHIPPLE, A. O. (1945) *Ann. Surg.*, 122, 449.

## Professor R. Milnes Walker:

**ABSTRACT.**—Portal obstruction may be intrahepatic or extrahepatic; in the latter case it is important to recognize the site; the diagnosis can best be confirmed by the demonstration of œsophageal varices, either by radiography or œsophagoscopy.

Estimation of the serum albumin gives the best indication of the state of liver function, and a level below 2.5 mg. % indicates that it is gravely impaired. Portal pressures up to 450 mm. of water have been found in the cases reported. A transverse upper abdominal incision gives good access and can be enlarged to the right for exposure of the portal vein, or to the left if a lieno-renal venous anastomosis is to be performed. As removal of the spleen entails removal of some of the collateral circulation, anastomosis between the portal vein and inferior vena cava is to be preferred when this is possible, but engorged veins around the portal vein may render this procedure impractical.

Of 19 patients, 4 have had no operation; in 5 cases splenectomy alone was performed, either because no splenic vein could be found, the vein was too friable for an anastomosis, or the patient was too shocked after splenectomy for anything further to be done. One patient had an omentopexy.

In 9 patients a venous anastomosis was performed; 7 had end-to-side lienorenal anastomosis and of them 3 died. The other 2 had anastomosis of the portal vein, with the inferior vena cava and right ovarian vein respectively with satisfactory results.

Résumé.—L'obstruction portale peut être intra ou extra-hépatique. Dans ce dernier cas il est important d'en reconnaître la localisation. Le diagnostic est établi le plus facilement par la démonstration radiologique ou œsophagoscopique de varices œsophagiennes. La détermination de l'albumine sérique est la meilleure mesure de la fonction hépatique, un niveau en dessous de 2.5 mg. pour cent indiquant une fonction gravement déficiente. Des pressions portales jusqu'à 250 mm. d'eau ont été observées dans les cas rapportés. Une incision transverse haute de l'abdomen donne une bonne voie d'accès, et peut être élargie vers la droite pour exposer la veine porte et vers la gauche pour permettre l'anastomose spléno-rénale. Comme la splénectomie entraîne l'élimination d'une partie de la circulation collatérale, il est préférable, si possible, de faire une anastomose entre la veine cave inférieure et la veine porte, mais l'engorgement des veines voisines à la veine porte peut rendre ce procédé impossible.

Sur 19 malades 4 n'ont pas été opérés, 5 ont été simplement splénectomisés, soit parce que la veine splénique n'a pas pu être trouvée, soit parce qu'elle était trop fragile pour permettre l'anastomose, soit parce que le malade était trop choqué pour permettre une intervention plus longue. Une omentopexie a été faite chez un malade.

Des anastomoses veineuses ont été faites dans 9 cas: spléno-rénales termino-latérales dans 7 cas dont 3 sont morts, et de la veine porte avec la veine cave inférieure dans un cas et avec la veine ovarienne dans un autre, avec des résultats satisfaisants.

КОНСПЕКТ.—Обструкция в воротной вене может быть внутри или вне-печеночная. При последней очень важно найти местоположение обструкции; диагноз может быть подтвержден определением варикозных узлов пищевода, либо радиологически, или при помощи энтерографии.

Определение сывороточного белка дает лучшее указание о состоянии почечной функции и уровень ниже 2.5 мг % доказывает серьезную недостаточность. В некоторых случаях давление в воротной вене достигало 450 мм воды. Поверхний разрез в верхней части живота дает хороший доступ и может быть удлинен вправо для сблизжения воротной вены, или-же влево, если нужно сделать селезеночно-почечный венозный анастомоз. В виду того, что при удалении селезенки приходится также удалить часть побочного кровообращения, анастомоз между воротной веной и нижней полой веной предпочтительнее, если это только возможно, но в некоторых случаях переполнение вен вокруг воротной вены делает это невозможным.

Из 19 пациентов четверо не было оперировано. Пятерым было сделано только удаление селезенки по той причине, что или селезеночная вена не была найдена, или-же эта вена была слишком хрупкая для анастомоза, или-же в виду того, что после удаления селезенки шок пациента не позволил продолжение операции. Одному больному была сделана спленопексия. В 9-ти случаях был сделан венозный анастомоз; из них семерым—селезеночно-почечный анастомоз/конец с концом/ и из них трое умерло; остальным двум был сделан анастомоз воротной вены в одном случае с нижней полой веной, а в другом с правой веной печени; результат был удовлетворительный.

RESUMEN.—La obstrucción portal puede ser intra o extra hepatica; en el segundo caso es importante el localizarla y la mejor manera de confirmar el diagnostico es comprobar la existencia de varices esofágicas, bien sea por radiología o por esofagoscopia.

El analisis de la albumina del suero es la mejor indicación del funcionamiento del higado y un nivel por debajo de 2.5 mg. por ciento indica que esta gravemente deteriorado. En los casos expuestos se han hallado presiones de hasta 450 mm. de agua. Una incisión transversal de la region abdominal superior da un buen acceso y se puede agrandar hacia la derecha para llegar a la vena porta, o hacia la izquierda si se intenta llevar a cabo la anastomosis lienorenal venosa. Como la extirpacion del bazo supone la eliminacion de una parte de la circulacion colateral, la anastomosis de la vena porta y la vena cava inferior es preferible siempre que esto sea posible, pero las venas congestionadas alrededor de la vena porta pueden hacer este procedimiento imposible.

De 19 pacientes cuatro no fueron operados; la esplenotomia se llevo a cabo solamente en cinco de los casos, bien porque no se pudo encontrar la vena esplenica o bien porque la

vena era demasiado delicada para una anastomosis o porque despues de la esplenotomia el paciente se hallaba en tal estado de shock que no fue posible hacer nada mas. A uno de los pacientes se le hizo una omentopexia.

En nueve de los pacientes se hizo una anastomosis venosa; a siete de ellos se les hizo una anastomosis lieno-renal de cabo a lado y de estos tres fallacieron. A los otros dos se les hizo la anastomosis de la vena porta con la vena cava inferior y con la vena ovarica del lado derecho respectivamente con resultados satisfactorios.

This paper is based on a small experience of 19 patients whom I have been asked to see during the last two years with a view to the establishment of a venous anastomosis in order to relieve the patient of the consequences of this high pressure.

These patients fall into two groups, those with normal livers and those with cirrhotic changes in that organ. The former group have been described as extrahepatic portal obstruction, but the block may actually be in the portal vein branches in the liver itself, but not in the liver parenchyma; the liver appears normal in every respect, and remains so though some of these patients have had their symptoms for years. The obstruction may be, as Whipple suggests, due to an extension of the obliterative process which occurs in the ductus venosus at birth, for most of these patients commence with symptoms early in life. In others the obstruction involves the splenic vein only, and such cases are cured by splenectomy alone, so they must be distinguished from the remainder; I have not encountered any such cases in this series.

Those with intrahepatic portal obstruction show considerable variation in the clinical picture; some have very large spleens and not very marked changes in the liver, others have gross cirrhosis without very much enlargement of the spleen, yet their portal pressure may be very high; in such patients ascites is often a prominent symptom, while in those with large spleens and less severe liver changes, œsophageal varices commonly draw attention to the presence of the disease.

The diagnosis of portal hypertension can best be made by the demonstration of œsophageal varices; these will usually show on examination by a barium swallow, but in a doubtful case examination with the œsophagoscope will be most valuable, and will sometimes demonstrate varices when the radiologist has failed to discover them.

As a next step it is most important to learn as much about the function of the liver as possible; this does not mean having all the liver function tests described in the books performed, for they will only contradict one another, but clinical examination, the complexion of the patient, the presence of ascites, jaundice, or œdema of the legs, will tell us a good deal. As regards biochemical tests, we have come to rely on the level of the serum albumin as the most valuable, and a better indication than the albumin-globulin ratio. Levels above 4 mg. % we consider very satisfactory, those below 3 mg. % as on the borderline, while for the moment if we find the serum albumin is consistently below 2.5 mg. % it is considered that the function of the liver is too much impaired to justify the risk of operation. Some evidence of the state of the liver may be obtained by performing a peritoneoscopy, and if necessary a biopsy may be taken by this method.

The level of portal venous pressure in our series has varied between 190 mm. and 450 mm. of water, but I have not enough data to correlate these with the symptoms.

When a decision has been made to operate, certain preparations are necessary; suitable blood for transfusion should be available, adequate diet with protein and glucose may help to make up deficiencies, and an intravenous pyelogram should be done to ensure that the kidneys are in the normal position and their function good.

As regards the operative approach, in many of our earlier patients we employed an incision through the left eleventh rib bed carried forward as far as the outer border of the rectus sheath; this was satisfactory for removal of the spleen, and gives an excellent approach to the left renal pedicle, but it is not easy to perform a liver biopsy through it, and close examination of the portal vein is impossible. More recently, therefore, we have adopted an upper abdominal transverse incision, which can be enlarged to either side, and even carried across the costal margin if necessary; thus either the portal vein and inferior vena cava on the one side, or the splenic and left renal veins on the other, can be approached. I have no experience of the right transthoracic approach to the inferior vena cava, but it certainly seems to offer possibilities of making the direct portal-caval anastomosis more feasible.

When the abdomen is open it is first important to establish the site of portal obstruction; cirrhosis of the liver may be recognized at once, but if the liver appears normal, it is necessary to examine the portal and splenic veins; that the obstruction is not limited to the splenic vein may be obvious by distended veins in the falciform ligament, or, as in a recent case, on the surface of the gall-bladder. If doubt still exists exposure of the portal vein and direct measurement of the pressure with a manometer attached to a needle in the vein should be undertaken.



The next step is to decide what sort of venous anastomosis is to be attempted, or if no such operation seems practical, whether an omentopexy should be done. In all these cases a free anastomosis has developed between the portal tributaries and the systemic circulation through the lieno-renal ligament, and around the tail of the pancreas; a splenectomy destroys a great part of this collateral circulation, whereas an attempt to establish a lieno-renal anastomosis may impair it still further by closing venous channels around the kidney. I have therefore come to the conclusion that where possible an anastomosis to the portal vein itself is the method of choice, for in addition to saving this collateral circulation, it does not submit the patient to the shock of what may be a very difficult splenectomy before the anastomosis is started. I therefore make a careful inspection of the portal vein; in some cases it is surrounded by a mass of small engorged vessels, and I have been unable to dissect it out on account of the free oozing from this area; under such conditions the site is abandoned and attention is turned to a lieno-renal anastomosis, but with experience I think it will be possible to use the portal vein in a greater proportion of cases, and with better results.

Four of our 19 patients have had no operation; in 3 cases it was thought that in the present state of our knowledge the hazards were too great to recommend it, though they have all had dangerous hæmorrhage from the œsophagus; 2 have had previous splenectomies, while the third is a child of 3½ years, and it is hoped to tide her over until she is a little older. In the fourth, it was clear that her serious symptoms were due to deficient liver function and not to portal hypertension, so surgical measures were not indicated. In the 15 operated upon, it has only been possible to perform a venous anastomosis in 9; of the remaining 6, 5 had a splenectomy alone, because in 2 no splenic vein could be found, in 2 this vein was so friable that sutures would not hold in it, and 1 was so shocked after splenectomy that it was not thought wise to continue. Two of this group died, one on the seventh, the other on the fourteenth day of liver failure. The sixth had had a previous nephrectomy, and as ascites was his only symptom, an omentopexy was performed.

Now we come to the 9 who have had a venous anastomosis. At the outset we aimed at avoiding the removal of a healthy kidney, so that in all these cases the kidney has been preserved; those who have had a lieno-renal anastomosis, 7 in all, have had a splenectomy followed by an end-to-side junction, with the exception of 1, in whom the renal vein was double, with a communicating channel close to the kidney, so here an end-to-end union was made to one of these veins. While performing the actual anastomosis a clamp should be placed on the renal artery, as well as those on the renal vein, otherwise gross congestion of the kidney occurs; we have had such clamps in place for up to eighteen minutes, without any evidence of impairment of renal function as shown by subsequent pyelograms. 3 of these 7 patients have died, 2 as a direct result of the operative intervention, for they leaked from the suture line, and perished on the first and third days respectively. The third death was due to mesenteric thrombosis three and a half weeks after operation; at the autopsy the branches of the portal vein in the liver were all blocked by old clot, and it seemed that all her portal blood had been returning through the anastomosis or through her collateral circulation, until shortly before her death. In the other 2 patients the portal vein has been used; one, a case of extrahepatic obstruction, had had a splenectomy three years previously, but hæmatemesis had recurred; here we were able to divide a large right ovarian vein, and implant its proximal end, by means of a metal cuff, into the side of the portal vein; she has remained symptom-free for more than a year, working in a factory, but her œsophageal varices are still present. The other patient was only operated on three weeks ago; he had hepatitis four years ago, and now has early cirrhosis, with a recent history of hæmatemesis. He is a thin man, and the exposure of his portal vein and of the vena cava was not difficult; temporary ligatures were placed round both these vessels, while a direct side-to-side anastomosis by means of sutures was performed, and thus the collateral circulation round his spleen has been undisturbed.

I have said nothing about the use of heparin, for my views are not yet crystallized; at the moment we commence giving it an hour or so after operation, and try to maintain a clotting time rather more than ten minutes for the next forty-eight hours, but if there is much oozing from the wound, in which a drain is always inserted, its administration is stopped at once.

We have at the moment no satisfactory way of knowing whether our anastomoses remain patent, but when we compare the after-histories of these patients with those in whom we have failed to complete the anastomoses, there is no doubt that on the whole they are benefited. If we are going to improve our results, it is important that we should operate early, before the liver function is greatly impaired, before there is a mass of engorged veins round the portal vein or related to the spleen, and before the vessel walls show evidence of degeneration; one attack of hæmatemesis from proved œsophageal varices should be considered an indication for exploration. It is far too early to assess the results, and in my hands the operation has not been without its tragedies, but I believe that it is designed on sound principles, and that experience, as in all other operations of surgery, will diminish its risks and clarify its indications.

**Mr. Donald Barlow:** Although much discussion has taken place as to the various methods by which portal hypertension may be relieved surgically, sufficient thought and study have not been given to the underlying pathology. Why do hepatic cirrhosis and portal vein thrombosis occur in the first place and what can be done to prevent their occurrence?

There is much evidence to show that in fact both conditions are metabolic diseases and may therefore be avoidable. So far as hepatic cirrhosis is concerned the work of Best, Haikoff, Connor and others has shown beyond doubt that, before their utilization, neutral fats are carried to the liver from storage depots and are there subjected to a process of phosphorylation. An essential link in this process is the choline molecule. If subjects receive a high fat or carbohydrate diet, the neutral fat (glyceride) content of the liver may be increased up to seventy times normal. If in these circumstances there is a deficiency in first-class protein intake and consequently a deficiency in choline in the diet there is a loss of the normal protective lipotropic effect of choline and the fat fatty liver remains. The fatty overloading by fat appears to cause a deficiency of oxygen consumption and the liver gradually becomes atrophied and fibrotic and may develop a cirrhosis of the Laennec type. In the fat fatty stage, for instance in pellagra, disappearance of the excess of fat may be obtained by feeding with choline or other lipotropic substances such as methionine or inositol, but once the disease is fully established and the liver fibrotic, the changes are irreversible.

The pathology of portal thrombosis is not so clearly understood but some interesting points emerge. First, except in cases due to injury, the initial thrombosis occurs in the portal and superior mesenteric veins and not in the splenic or gastric veins. The significance of this may be connected with the fact of the causative agent being of intestinal origin. Arterial venous anastomosis is often found at operation.

There is some evidence that atheroma is a deficiency disease associated with abnormal cholesterol metabolism. Also, on high cholesterol diet, a cholesterol-fatty liver can be produced with control by lipotropic substances. No definite conclusions can be drawn from these facts but further research on the subject is indicated.

With reference to short-circuit operations, 8 cases were studied and splenic-renal anastomosis carried out in 3 of them using the direct end-to-end operation in two instances and end-to-side in the third. The patients are completely relieved to date, i.e. for periods up to 10 years.

An attempt to treat a case of ascites by removing one kidney and anastomosing the renal pelvis to the peritoneum so that the ascitic fluid could drain down the ureter failed because omentum blocked the pelvis.

**Mr. Digby Chamberlain:** If there is a place for vascular anastomosis in the treatment of portal hypertension, it would seem that joining of the portal vein to the inferior vena cava would be more satisfactory than a lienorenal shunt. We find at operation that numerous large collaterals have been formed by nature in the abdominal wall, and in the retroperitoneal spaces, and on X-ray we see the veins in the walls of the oesophagus. Some of these are almost as large as the artificially made lienorenal anastomosis, which only adds one more vessel to the collateral circulation, whereas a portal-caval shunt diverts the whole of the portal blood to the systemic circulation and reduces the pressure to one comparable with the intra-caval pressure.

My experience, apart from splenectomy, is confined to 2 cases of portal-caval anastomosis, both of whom have recovered. In these cases I have used a right paramedian approach. The portal vein is defined from its formation behind the neck of the pancreas to its division into its right and left branches and any small veins entering it are doubly ligatured and divided. It will be found that the vein runs much more obliquely than might be expected. The vein is clamped and cut as near its division as possible. A side clamp is put on the inferior vena cava just below the renal veins, and an end-to-side anastomosis is carried out. In my first case I used a vitallium tube but had to complete the junction with silk sutures; in the second case I used direct suture. I have not used heparin in view of the large amount of oozing in the abdominal wall and in the mobilization of the duodenum.

My first case, a woman of 53, presented with gross ascites and hæmatemesis, and was operated on four months ago. Her liver was small and fissured. Her ascites has now disappeared. She has had no further bleeding and her liver is enlarged to 3 in. below her costal margin.

The second case, a man of 33, had his spleen removed in 1944, since when he has had numerous hæmorrhages. He was operated on one month ago, so that it is too early to say what the result will be.

The first case has gained weight, so that her nutrition does not seem to have suffered by cutting off her liver from the portal blood, and the increase in size of her liver is remarkable. It is difficult to assess the results at this early stage, but portal-caval anastomosis seems worth an extended trial, if the operative risk can be shown to be small.

The next step is to decide what sort of venous anastomosis is to be attempted, or if no such operation seems practical, whether an omentopexy should be done. In all these cases a free anastomosis has developed between the portal tributaries and the systemic circulation through the lienorenal ligament, and around the tail of the pancreas; a splenectomy destroys a great part of this collateral circulation, whereas an attempt to establish a lienorenal anastomosis may impair it still further by closing venous channels around the kidney. I have therefore come to the conclusion that where possible an anastomosis to the portal vein itself is the method of choice, for in addition to saving this collateral circulation, it does not submit the patient to the shock of what may be a very difficult splenectomy before the anastomosis is started. I therefore make a careful inspection of the portal vein; in some cases it is surrounded by a mass of small engorged vessels, and I have been unable to dissect it out on account of the free oozing from this area; under such conditions the site is abandoned and attention is turned to a lienorenal anastomosis, but with experience I think it will be possible to use the portal vein in a greater proportion of cases, and with better results.

Four of our 19 patients have had no operation; in 3 cases it was thought that in the present state of our knowledge the hazards were too great to recommend it, though they have all had dangerous hæmorrhage from the œsophagus; 2 have had previous splenectomies, while the third is a child of 3½ years, and it is hoped to tide her over until she is a little older. In the fourth, it was clear that her serious symptoms were due to deficient liver function and not to portal hypertension, so surgical measures were not indicated. In the 15 operated upon, it has only been possible to perform a venous anastomosis in 9; of the remaining 6, 5 had a splenectomy alone, because in 2 no splenic vein could be found, in 2 this vein was so friable that sutures would not hold in it, and 1 was so shocked after splenectomy that it was not thought wise to continue. Two of this group died, one on the seventh, the other on the fourteenth day of liver failure. The sixth had had a previous nephrectomy, and as ascites was his only symptom, an omentopexy was performed.

Now we come to the 9 who have had a venous anastomosis. At the outset we aimed at avoiding the removal of a healthy kidney, so that in all these cases the kidney has been preserved; those who have had a lienorenal anastomosis, 7 in all, have had a splenectomy followed by an end-to-side junction, with the exception of 1, in whom the renal vein was double, with a communicating channel close to the kidney, so here an end-to-end union was made to one of these veins. While performing the actual anastomosis a clamp should be placed on the renal artery, as well as those on the renal vein, otherwise gross congestion of the kidney occurs; we have had such clamps in place for up to eighteen minutes, without any evidence of impairment of renal function as shown by subsequent pyelograms. 3 of these 7 patients have died, 2 as a direct result of the operative intervention, for they leaked from the suture line, and perished on the first and third days respectively. The third death was due to mesenteric thrombosis three and a half weeks after operation; at the autopsy the branches of the portal vein in the liver were all blocked by old clot, and it seemed that all her portal blood had been returning through the anastomosis or through her collateral circulation, until shortly before her death. In the other 2 patients the portal vein has been used; one, a case of extrahepatic obstruction, had had a splenectomy three years previously, but hæmatemesis had recurred; here we were able to divide a large right ovarian vein, and implant its proximal end, by means of a metal cuff, into the side of the portal vein; she has remained symptom-free for more than a year, working in a factory, but her œsophageal varices are still present. The other patient was only operated on three weeks ago; he had hepatitis four years ago, and now has early cirrhosis, with a recent history of hæmatemesis. He is a thin man, and the exposure of his portal vein and of the vena cava was not difficult; temporary ligatures were placed round both these vessels, while a direct side-to-side anastomosis by means of sutures was performed, and thus the collateral circulation round his spleen has been undisturbed.

I have said nothing about the use of heparin, for my views are not yet crystallized; at the moment we commence giving it an hour or so after operation, and try to maintain a clotting time rather more than ten minutes for the next forty-eight hours, but if there is much oozing from the wound, in which a drain is always inserted, its administration is stopped at once.

We have at the moment no satisfactory way of knowing whether our anastomoses remain patent, but when we compare the after-histories of these patients with those in whom we have failed to complete the anastomoses, there is no doubt that on the whole they are benefited. If we are going to improve our results, it is important that we should operate early, before the liver function is greatly impaired, before there is a mass of engorged veins round the portal vein or related to the spleen, and before the vessel walls show evidence of degeneration; one attack of hæmatemesis from proved œsophageal varices should be considered an indication for exploration. It is far too early to assess the results, and in my hands the operation has not been without its tragedies, but I believe that it is designed on sound principles, and that experience, as in all other operations of surgery, will diminish its risks and clarify its indications.

## Section of Ophthalmology

President—CHARLES GOULDEN, O.B.E., M.A., M.D., F.R.C.S.

[February 11, 1949]

### The Retro-orbital Tissues as a Site of Outflow of Cerebrospinal Fluid

By E. J. FIELD, M.D., M.S., and J. B. BRIERLEY, M.D.

*Department of Anatomy, University of Bristol*

FOLLOWING the extensive researches of Weed (1914) it has been widely accepted that resorption of cerebrospinal fluid takes place mainly into the venous system. The lymphatic connexions of the subarachnoid space, other than those via the arachnoid sheaths of the olfactory nerves and the nasal mucosa, have received scant attention. The relatively few investigations to which they have been subject offer difficulties of interpretation because they were often carried out on the dead animal, (Schwalbe, 1869, 1870), and frequently, too, indicator material was introduced into the subarachnoid space under pressures greatly in excess of the normal. Moreover, when particulate material was employed no indication has been given of particle size. Following a review of the literature, the authors devised a method whereby indian ink, of particle size ranging between 0.5 and 1.5  $\mu$ , could be introduced into the cranial subarachnoid space of the living rabbit under conditions which precluded any rise of intracranial tension above the normal (Brierley and Field, 1948). Through a small burr hole in the parieto-occipital region cerebrospinal fluid was withdrawn from the cisterna magna or transverse fissure, and a syringe of sterile indian ink connected to the needle, the ink meniscus being about 120 mm. above the animal's skull. In this way ink was allowed to run in to replace the fluid withdrawn. When no more would run the needle was smartly withdrawn and the burrhole sealed with bone wax. The volume of ink introduced in this way was usually rather less than that of the fluid initially removed. The procedure was sometimes repeated on successive days when it was found that progressively smaller introductions could be achieved, but there was no rise in intracranial pressure.

Examination of animals at intervals of four to ninety-six hours after operation revealed an extensive communication between the spinal subarachnoid space and the prevertebral lymph nodes (Brierley and Field, 1948; Field and Brierley, 1948) and also between the cranial subarachnoid space and the lymphatic plexus of the nasal mucosa (Field, Brierley and Yoffey, 1949). The subarachnoid sleeve of the optic nerve, as might be expected, was well filled with ink. However, on removing the eyeball the retro-orbital fat was also found to be ink-stained. Further investigation of this outflow was facilitated by the use of albino animals in which the absence of pigment simplified the recognition of ink. This latter was found to accumulate in the fatty tissue around the optic nerve immediately behind the posterior pole of the eyeball and to spread laterally for a few millimetres in the episcleral plane. Viewed from the inside of the eye this gave the appearance of radiating black lines passing out from the optic nerve head. Ink permeated the retractor bulbi muscle and the extrinsic ocular muscles, particularly at their scleral attachments. Histological examination showed ink particles passing through the dura-arachnoid sheath of the optic nerve close behind the sclera and coming to lie in the adjacent fatty tissue (fig. 1). Whilst many particles were contained within macrophages, others were free and appeared to have passed directly through the dura-arachnoid. In meridional

Mr. Alan H. Hunt: My observations are based on the experience of 10 cases.

The nature of portal to systemic venous communications seems to differ in the two main types of portal obstruction. In cirrhosis hepatis no new channels of any size appear though existing channels become dilated. In the extrahepatic congenital type of portal block new channels develop which may become very large. This "cavernoma" formation does not resemble a cavernous hemangioma and must be distinguished from a true angioma such as was shown by Professor Learmonth. It is possible, on occasions, to use such dilated channels for short-circuiting the portal flow into the vena cava.

In both types the posterior parietal peritoneum becomes, to a greater or lesser extent, thickened and velvety with a feltwork of myriads of new vascular capillaries which extend up to the origin of the diaphragm but no farther. Diathermy coagulation is of great value in keeping the bleeding from these small channels under control. Omental adhesions become excessively vascular.

*Investigations.*—As one of the many routine investigations it would seem advisable to œsophagoscope and sigmoidoscope these patients, especially when the evidence points to an extrahepatic block. Sigmoidoscopy may be of value to distinguish obstruction in the splenic vein from that nearer the liver.

In taking portal pressures at operation the parts should be disturbed as little as possible. The readings obtained from different parts of the obstructed portal tree are found to vary little. Portal venograms I find unsatisfactory.

*Indications for operation.*—(a) *Hæmorrhage:* One severe hæmorrhage from an œsophageal or gastric varix makes an operation for the relief of portal hypertension imperative. I have lost a case from gastric hæmorrhage.

(b) *Ascites:* It is worth noting the brittleness of the veins in some cases of long-standing ascites. The portal vein can be handled with much greater ease than the splenic. The synchronous use of two small dissecting pellets is of great value in dissecting the veins, using one to steady the vein and the other to free it from its bed.

*Type of operation.*—The object is to relieve the portal hypertension; therefore, the largest possible stoma should be constructed. In cases with congenital extrahepatic block the portal vein, or one of its branches, is not readily available. Thus spleno-renal anastomosis is probably the best operation in these cases, preferably by end-to-side suture (Linton, R. R., Hardy, I. B., and Volwiler, W. (1948) *Surg. Gynec. Obstet.*, 87, 129). End-to-end anastomosis over a Blakemore-Lord tube necessitates sacrificing a kidney and the anastomosis is not so large. Many other less effective operations have been done.

In the cirrhotic cases I favour a portal-caval anastomosis-in-continuity, with incomplete transection of the portal vein.

My aversion to end-to-side portal-caval anastomosis is based on the hypothesis that, in cases of portal obstruction due to cirrhosis hepatis, the condition may progress to such an extent that the portal vein finally comes to act as a relief mechanism, the flow through it being reversed. This as yet cannot be proved, but the following evidence is sufficient to suggest that it is risky to divide the portal vein completely in advanced cases.

One patient, in whom the portal vein was divided (the hepatic end being ligated and the intestinal end anastomosed to the inferior vena cava), died on the sixth post-operative day in coma due to liver failure. At post-mortem the anastomosis was satisfactory, the intra-hepatic branches of the portal vein showed intense congestion, and the liver showed anoxic central lobular necrosis. At operation it had been noted that a raw area of liver had bled severely even after division of the portal vein, and that the hepatic artery was markedly hypertrophied. These findings suggested that the portal vein had been conducting blood away from the obstructed hepatic sinusoids.

Another patient, suffering from biliary cirrhosis, died of liver failure without operation. Post mortem perfusion of warm normal saline into the hepatic artery at 120 mm.Hg pressure had to be combined with a manometric pressure-head of 750 mm. water into the portal vein before the saline flowed into the hepatic veins. In a control experiment, 50 mm. water was sufficient. A carmine suspension perfused into the hepatic artery flowed back into the portal vein branches, against considerable pressure, the hepatic vein again remaining empty. (The highest pressure I have yet encountered in a case of portal hypertension at operation has been 440 mm. water.)

(Photographic illustrations of these findings were presented.)

To elucidate the further path which such retro-orbital ink might take, another series of experiments was undertaken. By means of a curved needle introduced through the superior conjunctival fornix, 0.5 ml. of ink was deposited close to the posterior pole of the eye. At intervals of twelve to twenty-four hours after operation the animals were sacrificed and examined. It was found that after some twenty-four hours the superior pole of the uppermost deep cervical lymph node had become ink-stained.

Semiserial celloidin sections of the whole orbital content failed to reveal true endothelial-lined lymphatic vessels, but showed that spread of ink particles took place along more or less definite lines through the fat. Columns of ink could be traced out through the orbital fissure into the deep pterygoid region where true lymphatics were present. Through these, ink was conveyed to the uppermost deep cervical gland. The appearance of a strand of ink in the orbital fatty tissue is shown in fig. 5. The passage of ink (and presumably also of fluid) from the retro-orbital tissue to the cervical lymphatic system is a slow process. It may be that the normal movements of the eyeball facilitate flow in much the same way as muscular contraction increases lymph flow in other parts of the body.

In none of our preparations was ink found within the retina or choroid. Likewise, under the given conditions, ink was never found to pass into the ocular fluids. Wegesfarth (1914), using the crystalloid Prussian blue mixture of Weed (1914), came to the conclusion that the "respective fluids of the brain and eye intermingle and mix" in the tissues of the optic nerve. When pressure in the eye was reduced by opening the aqueous, Prussian blue injected into the subarachnoid space was found to pass "beneath the sclera as far forward as the limbus". Histological investigation showed that the indicator was located between the choroid and sclera as far as the ciliary body. It is interesting to note, however, that in the contralateral intact eye the injection material "had gone forward only as far as the posterior pole of the bulb, where there was a very light blue haze around the orbital end of the nerve".

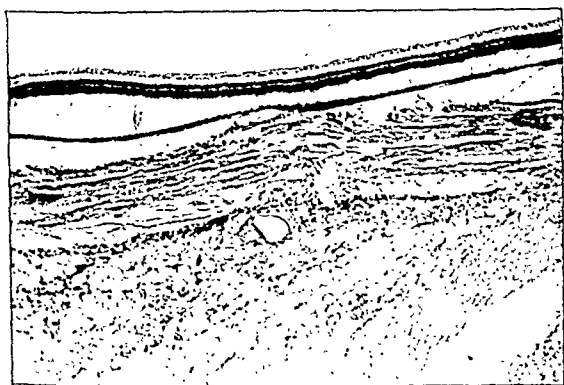


FIG. 3.

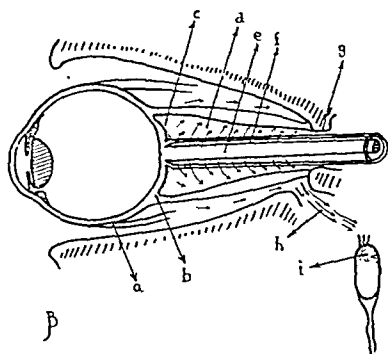


FIG. 6.

FIG. 3.—Ink particles are seen in the episcleral tissue some little distance lateral to the optic nerve head. Celloidin section.  $\times 48$ .

FIG. 6.—Diagram to illustrate the path taken by indian ink following its escape from the sheath of the optic nerve. a, extrinsic ocular muscle; b, retractor bulbi muscle; c, ink in the fat behind the posterior pole of the eye; d, ink passing out from the optic nerve sheath into the fat some little distance behind the nerve head; e, optic nerve; f, ink-filled extension of the subarachnoid space around the optic nerve; g, optic foramen; h, ink streaming out of orbital fissure; i, uppermost deep cervical lymph node showing ink in its superior pole.

section this migration of ink could be seen to extend some little way back along the optic nerve. In the retro-orbital fat there appeared more or less well-defined "fountains" of ink particles, though no endothelial-lined channels could be made out (fig. 2). Further spread in the episcleral plane is shown in fig. 3 where particles of ink are seen immediately outside the sclera several millimetres from the optic

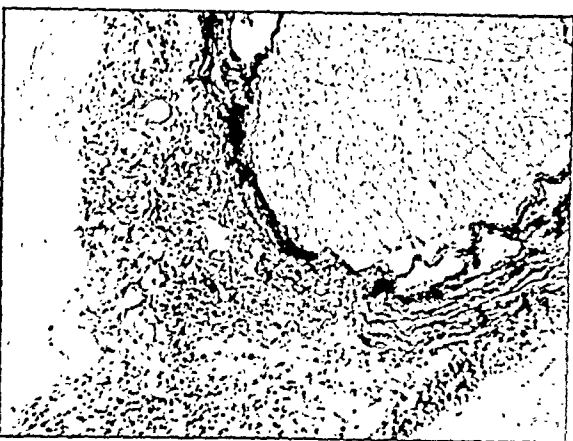


FIG. 1.

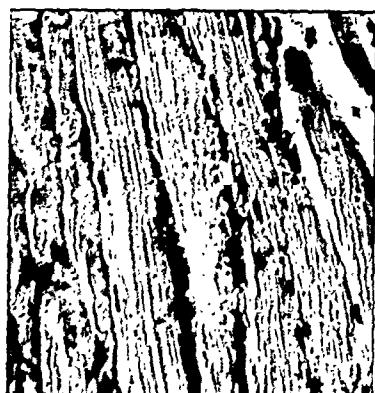


FIG. 4.

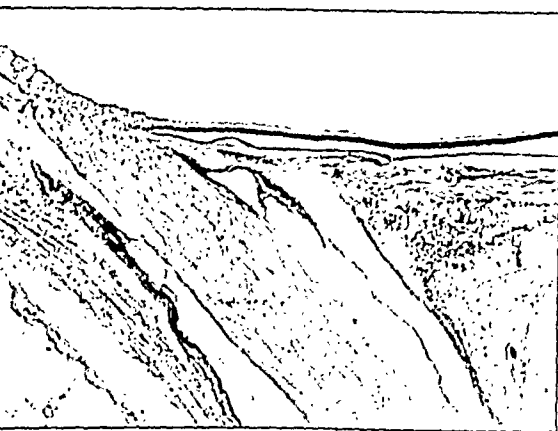


FIG. 2.



FIG. 5.

FIG. 1.—Transverse section through the optic nerve about 1 mm. behind the posterior pole of the eye. Above and to the right is the nerve, and particles of ink are seen to have passed through its dura-arachnoid sheath into the surrounding retro-orbital fat. Celloidin section.  $\times 35$ .

FIG. 2.—Meridional section of optic nerve head. On the right indian ink is seen to have escaped into the neighbouring fat and is making its way laterally in the episcleral plane. On the left ink is seen to have permeated the retractor bulbi muscle. Ink escape takes place for several millimetres behind the nerve head. Celloidin section.  $\times 15$ .

FIG. 4.—Particles of indian ink are seen streaming between muscle fibres of the retractor bulbi. Many of the particles are extracellular. Celloidin section.  $\times 225$ .

FIG. 5.—Strand of indian ink passing away from the optic nerve sheath through the orbital fat. The optic nerve is in the upper left corner of the figure. Celloidin section.  $\times 75$ .

nerve head. Microscopic examination of the retractor bulbi muscle showed particles of ink in columns between muscle fibres. Many particles were intracellular but some were still free (fig. 4).

[March 10, 1949]

## DISCUSSION ON OPHTHALMIC PHOTOGRAPHY

**Dr. Peter Hansell: Introduction.**—In this country, at the present time, there are at least seventy recognized medical photographic or illustration departments attached to hospitals or medical schools, and of these a large number have been established since the recent war. Pure ophthalmic photography has been practised only sporadically by these general departments, and such circumstances do not encourage proficiency. Considered as a specialized branch of medical photography, therefore, ophthalmic photography is still in an experimental stage, but capable of being developed within a group of eye hospitals. In the United States many such hospitals have had their own specialized departments for some time.

The fate and development of illustration services in ophthalmology, however, remain the responsibility of the medical staff, and it is only by an understanding of the techniques and media of illustration that intelligent usage can be achieved.

**Definition.**—The term "medical illustration" conveniently embraces photography, art-work and modelling, though in this discussion we are specifically concerned with the first of these.

**Basic equipment.**—A search through the literature reveals little in the way of specialized equipment, with the exception of three basic outfits which used to be manufactured by the firm of Zeiss; these demand some consideration:

(a) *The Zeiss Stereo-Iris Camera.*—Briefly, this is a camera having a pair of short focal-length lenses of fixed focus and aperture ( $F. = 5.5 \text{ cm.}, 1:6.3$ ). A large Compur-type shutter covers both lenses, but a pair of prisms in front of the lenses allow of almost co-axial illumination and visual focusing during the taking of the picture. With modern high-speed orthochromatic and panchromatic emulsions it is possible to use exposures in the region of  $1/50$ – $1/100$  sec., which demand little co-operation on the part of the patient. Photography in colour could probably be arranged by the use of longer exposures ( $1/10$ – $1$  sec.) or by the use of a flash-bulb as the source of illumination. A typical result is shown in fig. 1. However, the small field limited by the fixed working distance of the apparatus and the very shallow depth of focus remain inherent disadvantages.

(b) *The Zeiss-Nordenson Fundus Camera.*—Since its inception there have been two standard-models, differing mainly in the type of illuminant. The first of these embodied a carbon arc and suffered the drawback of recording appreciable corneal

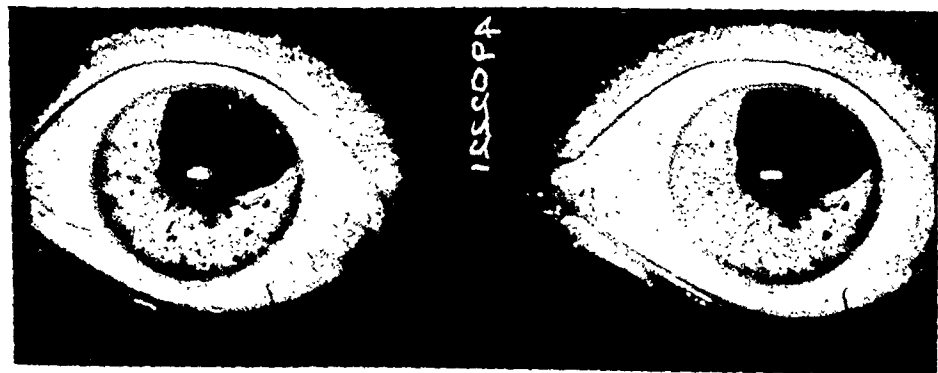


FIG. 1.—Result obtained with the Zeiss Stereo-iris Camera. Iridectomy: Melanoma left Iris.



Wustmann (1933) using thorotrast in the surviving dog found by X-ray examination that it could pass from the subarachnoid space to the back of the eyeball, and out towards the medial side of the eye. He describes the thorium as located "... epichoroideal in den Lymphräumen des Augenapfels". Further passage took place through perivascular spaces and "Lymphspalten". It is not clear from Wustmann's account whether strict precautions to prevent a rise in intracranial pressure were observed.

Schwalbe (1870) claimed to have demonstrated a connexion between the subarachnoid space and the perichoroidal space, though his experiments, carried out as they were on dead animals and at injection pressures of 60-80 mm.Hg, cannot be regarded as physiological. He found that Prussian blue could be induced to travel in the episcleral space as far as the venæ vorticosæ and thence into the perichoroidal space along the sheaths of these vessels. Whilst not denying that crystalloid material in the cerebrospinal fluid may indeed be induced to take the paths described by Schwalbe and Wegefarth, the authors believe that under normal conditions what small amount of fluid does escape into the retro-orbital fatty tissue takes the path indicated in fig. 6, to be absorbed finally into the cervical lymphatic system.

Brief reference may be made here to the work of Birch-Hirschfeld (1930) on the spread of indian ink in the retro-orbital tissues. He worked with living rabbits, monkeys and dogs and found ink to spread in the form of long branching strands apparently similar in appearance to those observed by us. In order to increase lymph flow in the orbit he treated some animals with dionin or paraphenylenediamine hydrochloride. Such animals developed exophthalmos because of the increased fluid in the retro-orbital fat, and when this tissue was examined histologically strands of indian ink were found to be confined largely to definite "Spalträume" or tissue spaces. Birch-Hirschfeld thought these spaces were lined by flattened endothelial cells but was not inclined to designate them true lymphatic vessels. The same appearances have been noted in our own material and they suggest that lines of least resistance serving as conduits for tissue fluid may exist between columns of fat cells. The flattened lining cells appear to be merely the nuclei of fat cells which chance to border on the fluid channel.

In conclusion, it may be pointed out that the outflow of cerebrospinal fluid (1) from the arachnoid cûls-de-sac around the spinal nerve roots, (2) from the arachnoid sheaths of the olfactory nerves, and (3) from the sheath of the optic nerve present certain features in common. In each case particles of ink make their way through a membrane to emerge in fatty areolar tissue outside: in the epidural fat of the intervertebral foramen, in the stroma of the nasal mucosa and in the retro-orbital fat respectively. In the two former situations true lymphatic channels are close at hand (Field and Brierley, 1948; Field, Brierley and Yoffey, 1949) so that but a small drift in tissue spaces need take place before the particles are collected into lymphatic radicles. In the case of the orbit, however, the fatty tissue surrounding the exit site of the ink is extensive and a slow, prolonged drift must occur before the nearest lymphatic vessels are reached.

#### REFERENCES

- BIRCH-HIRSCHFELD, A. (1930) *Handbuch der gesamten Augenheilkunde*. Berlin.  
 BRIERLEY, J. B., and FIELD, E. J. (1948) *J. Anat., Lond.*, 82, 153.  
 FIELD, E. J., and BRIERLEY, J. B. (1948) *J. Anat., Lond.*, 82, 198.  
 ———, ———, and YOFFEY, J. M. (1949) *J. Anat., Lond.*, 83, 77.  
 SCHWALBE, G. (1869) *Zbl. med. Wiss.*, 7, 465.  
 ——— (1870) *Archiv. mikr. Anat.*, 6, 1.  
 WEED, L. H. (1914) *J. med. Res.*, 31, 21.  
 WEGEFARTH, P. (1914) *J. med. Res.*, 31, 119.  
 WUSTMANN, O. (1933) *Dtsch. Z. Chir.*, 238, 529.

[March 10, 1949]

## DISCUSSION ON OPHTHALMIC PHOTOGRAPHY

**Dr. Peter Hansell: Introduction.**—In this country, at the present time, there are at least seventy recognized medical photographic or illustration departments attached to hospitals or medical schools, and of these a large number have been established since the recent war. Pure ophthalmic photography has been practised only sporadically by these general departments, and such circumstances do not encourage proficiency. Considered as a specialized branch of medical photography, therefore, ophthalmic photography is still in an experimental stage, but capable of being developed within a group of eye hospitals. In the United States many such hospitals have had their own specialized departments for some time.

The fate and development of illustration services in ophthalmology, however, remain the responsibility of the medical staff, and it is only by an understanding of the techniques and media of illustration that intelligent usage can be achieved.

**Definition.**—The term "medical illustration" conveniently embraces photography, art-work and modelling, though in this discussion we are specifically concerned with the first of these.

**Basic equipment.**—A search through the literature reveals little in the way of specialized equipment, with the exception of three basic outfits which used to be manufactured by the firm of Zeiss; these demand some consideration:

(a) *The Zeiss Stereo-Iris Camera.*—Briefly, this is a camera having a pair of short focal-length lenses of fixed focus and aperture ( $F. = 5.5 \text{ cm.}, 1:6.3$ ). A large Compur-type shutter covers both lenses, but a pair of prisms in front of the lenses allow of almost co-axial illumination and visual focusing during the taking of the picture. With modern high-speed orthochromatic and panchromatic emulsions it is possible to use exposures in the region of  $1/50$ – $1/100$  sec., which demand little co-operation on the part of the patient. Photography in colour could probably be arranged by the use of longer exposures ( $1/10$ – $1$  sec.) or by the use of a flash-bulb as the source of illumination. A typical result is shown in fig. 1. However, the small field limited by the fixed working distance of the apparatus and the very shallow depth of focus remain inherent disadvantages.

(b) *The Zeiss-Nordenson Fundus Camera.*—Since its inception there have been two standard models, differing mainly in the type of illuminant. The first of these embodied a carbon arc and suffered the drawback of recording appreciable corneal

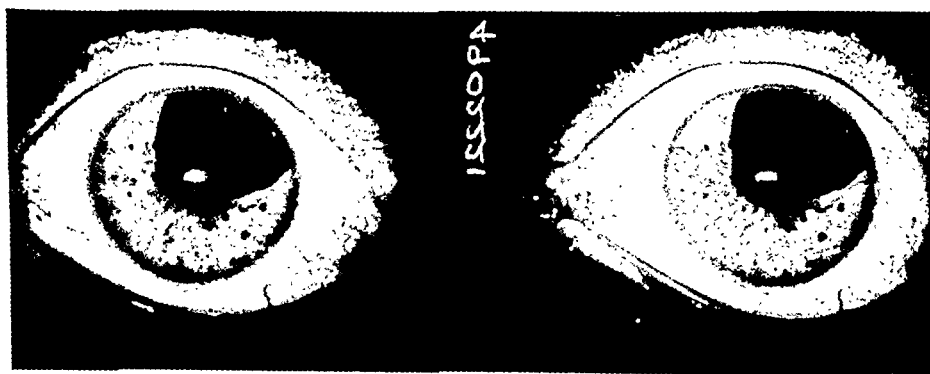


FIG. 1.—Result obtained with the Zeiss Stereo-iris Camera. Iridectomy: Melanoma left Iris.

reflexes. This model was later replaced by one using a Nitra-lamp with an annular filament and by a simple modification the small single reflex was eliminated. Despite various improvements, exposures with the newer model range from  $1/25$ – $1/5$  sec., even with the fastest monochromatic emulsions (fig. 2). Colour photography is therefore rather out of the question in view of the lengthy exposures which would be involved. By virtue of its highly concentrated light-source, however, the older carbon-arc model may still be used satisfactorily with colour materials: Bedell (U.S.A.) has produced a fairly complete set of fundus records in colour by this means.

A few of the workers in this country who are fortunate enough to possess a Zeiss-Nordenson Camera are contemplating the use of the electronic flash discharge tube as a source of illumination. Similar ideas have occurred in South America (Halberg, awaiting publication), but to date no results appear to have been published. This particular type of flash tube has many other possible applications to ophthalmic and general medical photography (*see under Illumination*).

(c) *The Zeiss Photo-Keratoscope* (Amsler).—This apparatus provides a means whereby corneal images of a Placido disc may be permanently recorded. The names of Amsler and Hartinger (Hartinger, 1930) are usually associated with the development of this equipment, but until recently it has not enjoyed universal popularity.

Photographic records produced by this means provide information concerning the geometric form of the cornea, and will also reveal any abnormalities of surface. With the renewed interest in corneal grafting, a greater demand for this type of photography may soon be shown.

The apparatus employs a disc of 14 cm. diameter, illuminated from behind by four 40 watt bulbs. The camera objective is situated in the centre of this disc and has a fixed working distance of about 6 cm. from the eye; hence all records are

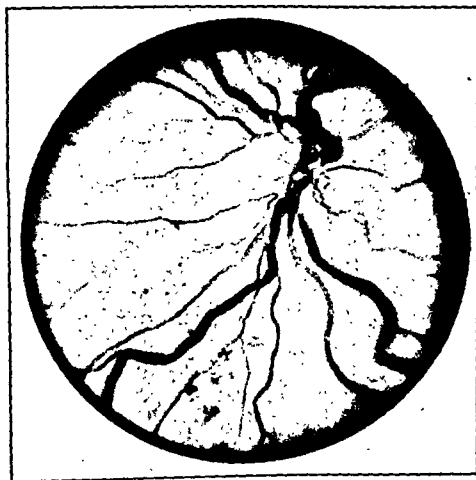


FIG. 2.—Photograph obtained with reflex-free Zeiss-Nordenson fundus camera. Lymphatic leukaemia.

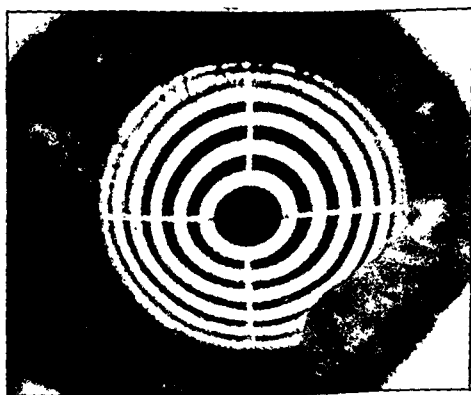


FIG. 3.—Record obtained with the Zeiss Photo-keratoscope in mild keratoconus (Amsler).

instantly comparable. Exposures are arranged to be less than 1 sec. on fast plates of size  $4.5 \times 6$  cm. A typical record is shown in fig. 3.

Within the last fifteen years the American firms of Bausch and Lomb and the Fairchild Aircraft Corporation have both produced special cameras for ophthalmic

work. The Anterior Segment Stereo Camera was designed by Bausch and Lomb primarily to photograph corneal abrasions and injuries sustained in industry: the records obtained were frequently used in connexion with claims and compensation. This camera was discontinued about 1940. At the time of writing, however, it is understood that this same firm has now perfected a new retinal camera which is due to be exhibited this year in June 1949. The Fairchild camera, which was equally short-lived, amounted to a low-power corneal microscope producing an enlarged image on a popular-sized roll film (Gartner, 1944). A condensed beam from a flat spiral discharge tube provided the intense light (two million international candles) required, exposure being determined by the length of the flash (1/15,000th sec.).

From the foregoing it will be seen that one of the chief problems confronting the ophthalmic photographer is the supply of equipment, for this must either be purchased through a very limited second-hand market or must be designed and constructed to order. Outside the limited scope of the Zeiss equipment, however, ophthalmic photography has everything in common with general medical photography—the equipment required and the uses of the finished products are exactly similar.

*Illumination.*—Lighting is perhaps the one factor in eye photography which demands special consideration. On this rests the comfort of the patient and his ability to co-operate; the clarity and depth of focus in the finished result; the presence or absence of disturbing highlights, and the ability to produce colour records of an



FIG. 4.—Flash photograph. Melanoma of right limbus.

irritable eye. Since most photography of the eye is of the close-up variety, necessitating long bellows extension, the intensity of illumination required is many times greater than that needed for general work. Add to this the fact that colour material is four or five times slower than the conventional monochromatic emulsions, and some idea of the problem may be formed.

reflexes. This model was later replaced by one using a Nitra-lamp with an annular filament and by a simple modification the small single reflex was eliminated. Despite various improvements, exposures with the newer model range from  $1/25$ – $1/5$  sec., even with the fastest monochromatic emulsions (fig. 2). Colour photography is therefore rather out of the question in view of the lengthy exposures which would be involved. By virtue of its highly concentrated light-source, however, the older carbon-arc model may still be used satisfactorily with colour materials: Bedell (U.S.A.) has produced a fairly complete set of fundus records in colour by this means.

A few of the workers in this country who are fortunate enough to possess a Zeiss-Nordenson Camera are contemplating the use of the electronic flash discharge tube as a source of illumination. Similar ideas have occurred in South America (Halberg, awaiting publication), but to date no results appear to have been published. This particular type of flash tube has many other possible applications to ophthalmic and general medical photography (*see under Illumination*).

(c) *The Zeiss Photo-Keratoscope* (Amsler).—This apparatus provides a means whereby corneal images of a Placido disc may be permanently recorded. The names of Amsler and Hartinger (Hartinger, 1930) are usually associated with the development of this equipment, but until recently it has not enjoyed universal popularity.

Photographic records produced by this means provide information concerning the geometric form of the cornea, and will also reveal any abnormalities of surface. With the renewed interest in corneal grafting, a greater demand for this type of photography may soon be shown.

The apparatus employs a disc of 14 cm. diameter, illuminated from behind by four 40 watt bulbs. The camera objective is situated in the centre of this disc and has a fixed working distance of about 6 cm. from the eye; hence all records are

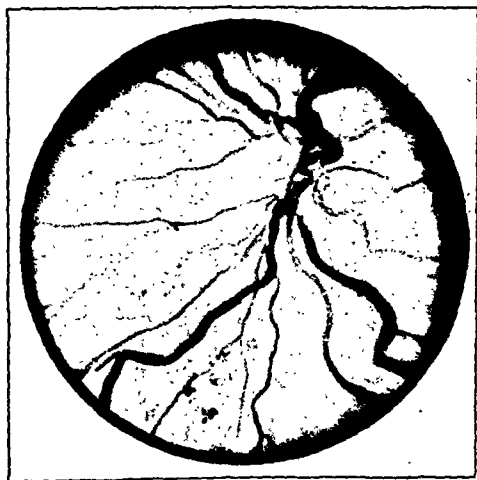


FIG. 2.—Photograph obtained with reflex-free Zeiss-Nordenson fundus camera. Lymphatic leukaemia.

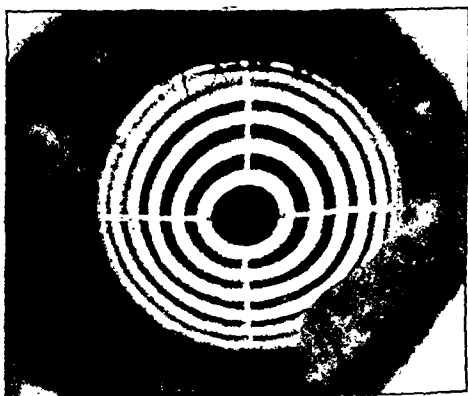


FIG. 3.—Record obtained with the Zeiss Photo-keratoscope in mild keratoconus (Amsler).

instantly comparable. Exposures are arranged to be less than 1 sec. on fast plates of size  $4.5 \times 6$  cm. A typical record is shown in fig. 3.

Within the last fifteen years the American firms of Bausch and Lomb and the Fairchild Aircraft Corporation have both produced special cameras for ophthalmic

work. The Anterior Segment Stereo Camera was designed by Bausch and Lomb primarily to photograph corneal abrasions and injuries sustained in industry: the records obtained were frequently used in connexion with claims and compensation. This camera was discontinued about 1940. At the time of writing, however, it is understood that this same firm has now perfected a new retinal camera which is due to be exhibited this year in June 1949. The Fairchild camera, which was equally short-lived, amounted to a low-power corneal microscope producing an enlarged image on a popular-sized roll film (Gartner, 1944). A condensed beam from a flat spiral discharge tube provided the intense light (two million international candles) required, exposure being determined by the length of the flash (1/15,000th sec.).

From the foregoing it will be seen that one of the chief problems confronting the ophthalmic photographer is the supply of equipment, for this must either be purchased through a very limited second-hand market or must be designed and constructed to order. Outside the limited scope of the Zeiss equipment, however, ophthalmic photography has everything in common with general medical photography—the equipment required and the uses of the finished products are exactly similar.

*Illumination.*—Lighting is perhaps the one factor in eye photography which demands special consideration. On this rests the comfort of the patient and his ability to co-operate; the clarity and depth of focus in the finished result; the presence or absence of disturbing highlights, and the ability to produce colour records of an

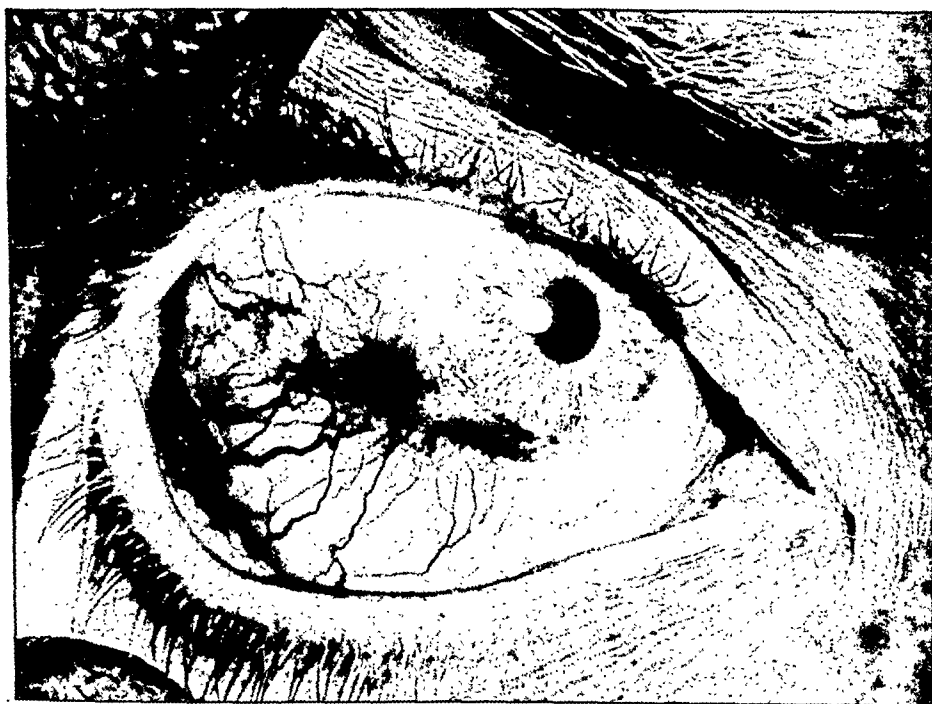


FIG. 4.—Flash photograph. Melanoma of right limbus.

irritable eye. Since most photography of the eye is of the close-up variety, necessitating long bellows extension, the intensity of illumination required is many times greater than that needed for general work. Add to this the fact that colour material is four or five times slower than the conventional monochromatic emulsions, and some idea of the problem may be formed.

For all intents and purposes the light sources available for this type of work may be subdivided as follows:

(a) Ordinary tungsten illumination consisting of incandescent bulbs of the order of 500 watts.

(b) Photoflood bulbs, which are essentially low-voltage bulbs overrun to a greater or lesser extent. They are, therefore, fairly short-lived when used continuously.

(c) Flash-bulbs, filled with magnesium alloy foil or wire. These give an intense single flash and are then expended.

(d) Electronic flash. This recent innovation consists of an argon-filled tube through which a high-voltage current is momentarily discharged from a bank of condensers. The light emission is of a constant quality and of extremely short duration (1/20,000th sec.). Each tube may be used for several thousand flashes.

Briefly, both tungsten and photoflood illumination are hot and uncomfortable for the patient when used at the levels required for short exposures (1/10th sec.). Furthermore, great care must be exercised when this lighting is used in conjunction with colour film, for slight voltage variations will often produce a marked effect on final colour balance.

Flash illumination has a great deal to commend it in this connexion. Its unpleasant effects are momentary, and it provides an extremely portable light-source for nearly every type of work and condition. Flash-bulbs are expensive, however, and are likely to remain so: the cost of illumination may therefore be as high as that of the photographic materials and labour (fig. 4).

Electronic flash, on the other hand, is likely to become almost ideal in the future. At the present time the initial expenditure on equipment is heavy, and the apparatus itself must be bulky to be efficient. American workers have used this type of lighting for some little time and with considerable effect. British equipment is still in a developmental stage, but the industry is making rapid progress. Regarding both this type of lamp and the flash-bulb, it should be mentioned that some little experience is necessary before the effect of any given placement of lamps can be predicted with certainty. Many of the larger tubes carry a built-in pilot lamp to assist in this primary positioning.

The above remarks apply mainly to still photography, and the illumination by flash does not provide an answer to the problems of cine-photography in colour. The normal projection and taking speed of cine-film is 16 frames/sec.: this predetermines the camera shutter speed at about 1/30th sec. Even using fast lenses with apertures ranging from *f* 1.5 to *f* 2.8, the level of illumination required for colour motion picture work may prove trying even to normal eyes. This factor should be borne in mind when making any request for a cine record involving an ocular lesion.

*Applications and uses.*—Having assembled photographic and illustrative matter, the uses to which it may be put are varied but straightforward. The applications of visual material have been listed in detail many times, but for our purposes they may be summarized as follows:

(1) CLINICAL—Recording stages or events in the natural history of a disease. An aid to the assessment of progress or treatment.

(2) RESEARCH—Recording of results for analysis and/or publication.

(3) EDUCATION—Visual media of instruction: e.g. display, lantern-slide, filmstrip, film, &c.

The simplest application of illustrative material to medical education is the static display. Apart from a few outstanding collections, such as the Wellcome Foundation Museum, this medium has been sadly neglected in this country. Admittedly, the initial collation of material and its lay-out demand time and patience, but the final result may be used time and again with the minimum of revision.

The filmstrip and the miniature lantern-slide (Hansell, 1949) also have a great potential future in this field. By definition, the filmstrip is an orderly sequence of still pictures on 35 mm. film and, although it should be prepared with the care of a motion picture, it is a vastly cheaper medium for the presentation of non-kinetic subjects. Furthermore, the teacher is able to control the tempo of projection and the sequence of his material will always be correct.

The miniature lantern-slide is derived from the filmstrip or vice versa. Complete flexibility of presentation is therefore achieved, and it is through this latter medium that inexpensive slides in full colour may be produced (fig. 6). Though primarily intended for projection, desk-type viewers are available for the individual inspection of such slides.

Enough has been written about medical film to fill many chapters, but the general standard of film production remains very low (Scientific Film Association, 1946), and teachers must be prepared to spend several months over the initial scripting; the present tendency is to decide to make a film but a week or two before an important lecture, subsequent imperfections being excused for this very reason. All these points have been mentioned elsewhere with greater clarity, but they must apply with equal force to ophthalmology.

(At the meeting of the Ophthalmological Section on March 10, 1949, two short films were shown: (a) "Some Uses of Film in Ophthalmology", produced by the Illustration Departments of Westminster Hospital and the Institute of Ophthalmology and (b) "Eversion of the Upper Eyelid", a short technique film produced by Dr. Brian Stanford.)

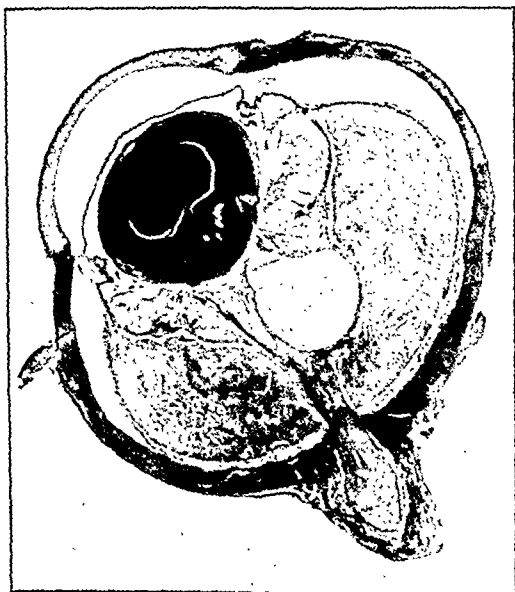


FIG. 5.—Photomicrograph—section of eye:  
Pseudoglioma.

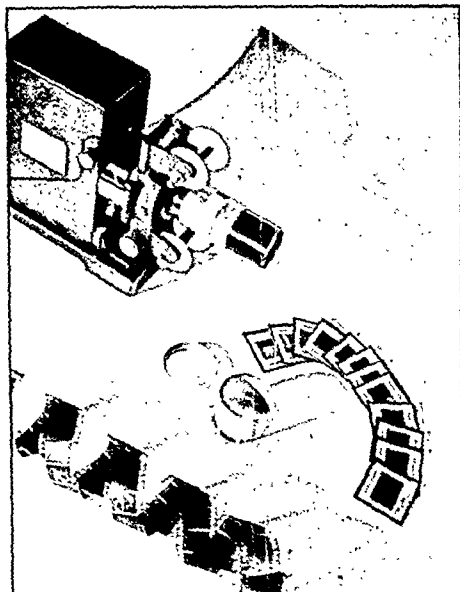


FIG. 6.—35 mm. filmstrip and slide projector.

*Comment.*—Most medical teachers and authors have very clear ideas concerning the illustrative material they wish to use. In general, their notions of the limitations and possibilities of the illustrative media are less formed, and it is probably for this reason that photographic and other services are often wastefully used. Medical illustration provides a very real supplement to the written or spoken word, but it must still be regarded as an expensive luxury.



There are certain basic questions which must be decided in advance: Is it a photograph which is required or would a line-drawing be more lucid? Is colour really an important feature? Is the subject essentially kinetic or static? How much information may be put on a single lantern-slide? Given the opportunity, most medical artists or photographers are in a position to offer sound advice, based on their previous successes and failures. A great deal of help, however, may be afforded by the medical staff when making requests for illustrations. Explicit instructions and thumbnail sketches to indicate positions required are of inestimable value to the photographer or artist. Too often does the phrase "Photograph please" appear on request cards, adequate instructions only rarely being appended.

#### SUMMARY

The basic equipment required for ophthalmic photography is described together with certain technical data. Methods of illumination are discussed in relation to the comfort of the patient and the quality of the finished result. Finally, the various illustrative media are reviewed, and some guiding principles for their considered use are laid down.

In conclusion, I would like to express my thanks to the staff of the Medical Illustration Department, Institute of Ophthalmology, and the Department of Medical Photography, Westminster Hospital, for their help in the assembly and presentation of this material.

#### REFERENCES

- GARTNER, S. (1944) *Arch. Ophthalm.*, 32, 464.  
HALBERG, Brit. J. *Ophthalm.*, awaiting publication.  
HANSELL, P. (1949) 35 mm. Filmstrip Technique. Ilford, London.  
HARTINGER, H. (1930) Ein neues Photokeratoskop. *Ber. Dtsch. ophth. Ges.*, 48, 360.  
The Place of the Film in Medical Education: Scientific Film Associations, 1946. London.  
WÜRTH (1948) Die Photographie in der Augenheilkunde: *Camera*, No. 6, June.

Mr. Edgar Fincham said that he was not an ophthalmologist but was something of a photographer and interested in optical technique. The photographs he had to show were not put forward as outstanding examples of pathological conditions but because most of them had been obtained with rather unusual methods of illumination in order to record things which perhaps were not ordinarily seen. His photographs had more to do with the physiology of the eye than with the recording of pathological states.

His first photograph of the eye was taken about twenty-five years ago and he thought it was the most ambitious effort he had ever made. It was undertaken to try to relieve the monotony of a Paper on the mechanism of accommodation. He thought it might be interesting to try to record the changes in the Purkinje images photographically. This meant studying a number of cases because the definition of the images varied from one case to another, but he found one subject which showed the images very well and he was able to get some photographs. For this purpose he used three sources of light in the form of a triangle. The illumination was obtained from an open arc lamp with three concave mirrors focusing the light on to the eye, and by means of a shutter in front of the lamp and a shutter on the camera, working more or less synchronously, it was possible to get photographs with the pupil dilated as in darkness.

Photographs had also been made with slit-lamp illumination. There were some difficulties in undertaking this but he thought it was well worth while trying. The slit-lamp was able to show so much that could not be seen otherwise. It was easy to illustrate the treatment or correction of a case of conical cornea by means of the contact lens. As a control he showed a normal cornea and compared this with the conical cornea with its opaque centre and again with the conical cornea fitted with the contact lens in position. It was intended that the contact lens should touch the centre of the cornea in the hope that it would prevent it coming forward any more. Some months after it was originally photographed he obtained some further photographs and was surprised to find that the spherical lens was then in contact with the cornea over practically the whole of the surface. One interesting point was that, as it seemed to him, this cornea was not thinner in the centre than the normal, but it was thicker at the margins.

Slit-lamp illumination showed remnants of the pupillary membrane. There was no other way of showing these, which were quite invisible with the ophthalmoscope but showed very clearly with the slit-lamp. In the illustration of congenital coloboma (fig. 1) the lamp was well over to the side. The tilt was made in order to show the pupillary fibre which was ordinarily not seen against the dark background of the pupil. It was shown quite clearly by direct illumination with slit-lamp.

Most of his slit-lamp photographs were taken to illustrate the changes in accommodation. One remarkable case of aniridia was included. The photograph here was taken from below at an angle of about 30 degrees. By an optical trick he was enabled to get a projection of these images to show the perpendicular view (fig. 2). It was a question of projecting the image back into the same position as was occupied by the eye at the time, and then placing a photographic plate in that position.



FIG. 1.—Remnant of pupillary membrane, slit-lamp section. Case of congenital coloboma.



(a)



(b)

FIG. 2.—Slit-lamp sections of crystalline lens in aniridia corrected to give perpendicular view. (a) Unaccommodated. (b) Accommodated. (Reproduced by permission *Trans. Ophthal. Soc., U.K.*)



(a)



(b)

FIG. 3.—Crystalline lens and ciliary body transilluminated in a case of gross detachment of iris. (a) Unaccommodated. (b) Accommodated.

Another method of photographing the eye which was not usually practised but was a perfectly good one was to adopt a procedure in which a plus lens was used and to observe the media by transillumination. Just as that was effective in the ophthalmoscope so it could be used in photography. He had used it only for recording the changes in the crystalline lens during accommodation in cases of aniridia or very large coloboma.

The next case he illustrated was one of very large detachment of the iris (fig. 3). The pupil was just visible. The iris was receiving a great deal of illumination, but the result showed quite nicely the change

There are certain basic questions which must be decided in advance: Is it a photograph which is required or would a line-drawing be more lucid? Is colour really an important feature? Is the subject essentially kinetic or static? How much information may be put on a single lantern-slide? Given the opportunity, most medical artists or photographers are in a position to offer sound advice, based on their previous successes and failures. A great deal of help, however, may be afforded by the medical staff when making requests for illustrations. Explicit instructions and thumbnail sketches to indicate positions required are of inestimable value to the photographer or artist. Too often does the phrase "Photograph please" appear on request cards, adequate instructions only rarely being appended.

#### SUMMARY

The basic equipment required for ophthalmic photography is described together with certain technical data. Methods of illumination are discussed in relation to the comfort of the patient and the quality of the finished result. Finally, the various illustrative media are reviewed, and some guiding principles for their considered use are laid down.

In conclusion, I would like to express my thanks to the staff of the Medical Illustration Department, Institute of Ophthalmology, and the Department of Medical Photography, Westminster Hospital, for their help in the assembly and presentation of this material.

#### REFERENCES

- GARTNER, S. (1944) *Arch. Ophthalm.*, **32**, 464.  
HALBERG. *Brit. J. Ophthalm.*, awaiting publication.  
HANSELL, P. (1949) 35 mm. Filmstrip Technique. Ilford, London.  
HARTINGER, H. (1930) Ein neues Photokeratoskop. *Ber. Dtsch. ophth. Ges.*, **48**, 360.  
The Place of the Film in Medical Education: Scientific Film Associations, 1946. London.  
WÜRTH (1948) Die Photographie in der Augenheilkunde: *Camera*, No. 6, June.

Mr. Edgar Fincham said that he was not an ophthalmologist but was something of a photographer and interested in optical technique. The photographs he had to show were not put forward as outstanding examples of pathological conditions but because most of them had been obtained with rather unusual methods of illumination in order to record things which perhaps were not ordinarily seen. His photographs had more to do with the physiology of the eye than with the recording of pathological states.

His first photograph of the eye was taken about twenty-five years ago and he thought it was the most ambitious effort he had ever made. It was undertaken to try to relieve the monotony of a Paper on the mechanism of accommodation. He thought it might be interesting to try to record the changes in the Purkinje images photographically. This meant studying a number of cases because the definition of the images varied from one case to another, but he found one subject which showed the images very well and he was able to get some photographs. For this purpose he used three sources of light in the form of a triangle. The illumination was obtained from an open arc lamp with three concave mirrors focusing the light on to the eye, and by means of a shutter in front of the lamp and a shutter on the camera, working more or less synchronously, it was possible to get photographs with the pupil dilated as in darkness.

Photographs had also been made with slit-lamp illumination. There were some difficulties in undertaking this but he thought it was well worth while trying. The slit-lamp was able to show so much that could not be seen otherwise. It was easy to illustrate the treatment or correction of a case of conical cornea by means of the contact lens. As a control he showed a normal cornea and compared this with the conical cornea with its opaque centre and again with the conical cornea fitted with the contact lens in position. It was intended that the contact lens should touch the centre of the cornea in the hope that it would prevent it coming forward any more. Some months after it was originally photographed he obtained some further photographs and was surprised to find that the spherical lens was then in contact with the cornea over practically the whole of the surface. One interesting point was that, as it seemed to him, this cornea was not thinner in the centre than the normal, but it was thicker at the margins.

# PROCEEDINGS *of the* ROYAL SOCIETY OF MEDICINE

ISSUED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE

HONORARY EDITORS

ERIC A. CROOK      E. R. CULLINAN

EDITOR

J. M. BROWNE KUTSCHBACH

|                                           |                                 |
|-------------------------------------------|---------------------------------|
| G. S. W. ORGANE (Anæsthetics)             | F. T. RIDLEY (Ophthalmology)    |
| J. S. RICHARDSON (Clinical)               | H. L.-C. WOOD (Orthopædics)     |
| J. B. BROOKSBY (Comparative Medicine)     | C. S. HALLPIKE (Otolary)        |
| E. W. PROSSER THOMAS (Dermatology)        | A. G. SIGNY (Pædiatrics)        |
| E. F. SCOWEN (Endocrinology)              | F. R. SELBIE (Pathology)        |
| ALLAN McFARLAN (Epidem. & State Med.)     | M. B. RAY (Physical Medicine)   |
| A. C. WHITE (Exper. Med. & Therap.)       | O. V. LLOYD-DAVIES (Proctology) |
| I. E. McCracken (History of Medicine)     | DENIS HILL (Psychiatry)         |
| W. A. MILL (Laryngology)                  | F. CAMPBELL GOLDING (Radiology) |
| MAURICE DAVIDSON (Medicine)               | CHARLES DONALD (Surgery)        |
| J. St. C. ELKINGTON (Neurology)           | G. M. FINDLAY (United Services) |
| LESLIE WILLIAMS (Obstetrics & Gynæcology) | A. CLIFFORD MORSON (Urology)    |
| B. W. FICKLING (Odontology)               |                                 |

SECRETARY OF THE ROYAL SOCIETY OF MEDICINE

G. R. EDWARDS

---

All communications concerning Editorial Business should be addressed to  
THE HONORARY EDITORS, 1, WIMPOLE STREET, LONDON, W.1

in diameter of the crystalline lens and also the movements of the ciliary processes. A similar photograph of a large coloboma did not record the diameter of the lens, but the movement of the ciliary processes was shown quite well. Another feature which was shown was the little crenations on the edge of the lens, apparently due to tension of the fibres. These tended to flatten out when the tension upon the lens was relaxed in accommodation. There was one great difficulty about this photography and that was the enormous range of brightness against which one had to contend. It was necessary to have a considerably flattened result, otherwise some parts such as the cornea and certainly the iris would be so intensely bright as to be unprintable.

Finally, Mr. Fincham briefly described his apparatus, most of which he had constructed himself, and he also showed an unusual photograph of a retinal image taken through an optometer.

Mr. Arthur Lister said that it was only proper that a clinician should make some contribution to the discussion. In actual fact he need not say very much because many of the clinical applications of photography were already familiar to those present. Clinical photography was still in its infancy in ophthalmology as well as in other specialties. It would grow only with extended use and he felt more use should be made of it. By this he did not mean that every squint should be photographed before and after operation but to take two small examples, more use could be made of photographs as records of growths, and, secondly, nothing could compare with colour photographs recording external conditions. He knew of no collection of colour photographic slides of external conditions in this Country such as he had seen in Brussels or in Calcutta; every eye department might well take a series of colour photographs of common eye diseases for teaching purposes.

His own particular interest was in fundus photography. Although fundus photography had reached a standard which made it of practical value, it still had some way to go before it achieved its full usefulness. One of the chief problems was exposure time. In the case of black-and-white photography an exposure of  $1/10$ th sec. gave good results, but in colour photography—especially as the standard of colour films had dropped since the war—it was necessary to give, so he understood, a  $\frac{1}{2}$  sec. exposure, and with the likelihood of movement of the eye of the patient, success was not obtained in more than 1 out of 3 or more exposures. This problem might be overcome by fitting to the fundus camera an electronic flash tube which gave an illumination of several thousand foot-candles. This would allow of an exposure of a few thousandths of a second.

Mr. Lister said that in selecting the photographs shown at the Meeting and, looking through the case-records attached to them, he was struck with the great possibilities which such photographs offered not only for teaching purposes but for the study of the ophthalmological aspects of systemic disease. He reminded the Section of the many varieties of retinal vascular change and of the value of having photographs of the fundus, taken at intervals in the course of a disease. The study of such a series might go a long way to solving some of the problems of the retinopathies and their causes. One wondered what Bright would have thought of it: the speaker then showed two illustrations of the fundus in Bright's disease. The first was a drawing made about 1860 soon after the ophthalmoscope was invented and the other was a recent photograph.

Mr. Fincham, speaking on the matter of exposures for fundus photograph which had been raised by Mr. Lister, said that with the use of the arc-lamp for monochrome photography an exposure of  $1/50$ th sec. did quite well. During his earlier remarks he had shown a Kodachrome which had received  $1/5$ th of a sec. Before the war an exposure of  $1/10$ th sec. for colour work could be given. But  $1/50$ th sec. for monochrome work was quite good.

Mr. B. W. Rycroft said that he had one or two examples taken by a method which Mr. Lister had mentioned, namely, the electronic flash. This was used for external records and for the recording of an operation. Some difficulty was present in getting rid of the highlights. His subjects included a pre-operative view of a graft case with a central nebula; also a case of cantho-rhinostomy. He showed a series of pictures of the operation.

Mr. Lister wondered if the arc-lamp might not give unpleasant after-images. He himself used a filament lamp with which he could take several photographs, with only a very short after-image. He thought that the arc-lamp might be rather troublesome in this respect.

Mr. Fincham said that he had not found this to be so. He had used the arc on his colleagues and there had been no complaints from them. He had been interested in the suggestion as to the use of the light of the electronic flash for fundus photography. Unless one could form an optical image which was quite small he wondered whether this presented any advantage. It was a question of just masking it down for the size required. The great advantage of the arc was that it was a very small and intense source. The filament lamp embodied a special circular filament, and he wondered how one managed with the image when the light was from a fairly large source.

Mr. Lister said that, on the point mentioned by Mr. Fincham, methods of masking had been applied. It did not matter much about wasting the light so long as the exposure could be cut to a sufficiently short time.

# PROCEEDINGS *of the* ROYAL SOCIETY OF MEDICINE

ISSUED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE

HONORARY EDITORS

ERIC A. CROOK      E. R. CULLINAN

EDITOR

J. M. BROWNE KUTSCHBACH

|                                           |                                 |
|-------------------------------------------|---------------------------------|
| G. S. W. ORGANE (Anæsthetics)             | F. T. RIDLEY (Ophthalmology)    |
| J. S. RICHARDSON (Clinical)               | H. L.-C. WOOD (Orthopædics)     |
| J. B. BROOKSBY (Comparative Medicine)     | C. S. HALLPIKE (Otiology)       |
| E. W. PROSSER THOMAS (Dermatology)        | A. G. SIGNY (Pædiatrics)        |
| E. F. SCOWEN (Endocrinology)              | F. R. SELBIE (Pathology)        |
| ALLAN McFARLAN (Epidem. & State Med.)     | M. B. RAY (Physical Medicine)   |
| A. C. WHITE (Exper. Med. & Therap.)       | O. V. LLOYD-DAVIES (Proctology) |
| I. E. McCRACKEN (History of Medicine)     | DENIS HILL (Psychiatry)         |
| W. A. MILL (Laryngology)                  | F. CAMPBELL GOLDING (Radiology) |
| MAURICE DAVIDSON (Medicine)               | CHARLES DONALD (Surgery)        |
| J. St. C. ELKINGTON (Neurology)           | G. M. FINDLAY (United Services) |
| LESLIE WILLIAMS (Obstetrics & Gynæcology) | A. CLIFFORD MORSON (Urology)    |
| B. W. FICKLING (Odontology)               |                                 |

SECRETARY OF THE ROYAL SOCIETY OF MEDICINE

G. R. EDWARDS

in diameter of the crystalline lens and also the movements of the ciliary processes. A similar photograph of a large coloboma did not record the diameter of the lens, but the movement of the ciliary processes was shown quite well. Another feature which was shown was the little crenations on the edge of the lens, apparently due to tension of the fibres. These tended to flatten out when the tension upon the lens was relaxed in accommodation. There was one great difficulty about this photography and that was the enormous range of brightness against which one had to contend. It was necessary to have a considerably flattened result, otherwise some parts such as the cornea and certainly the iris would be so intensely bright as to be unprintable.

Finally, Mr. Fincham briefly described his apparatus, most of which he had constructed himself, and he also showed an unusual photograph of a retinal image taken through an optometer.

Mr. Arthur Lister said that it was only proper that a clinician should make some contribution to the discussion. In actual fact he need not say very much because many of the clinical applications of photography were already familiar to those present. Clinical photography was still in its infancy in ophthalmology as well as in other specialties. It would grow only with extended use and he felt more use should be made of it. By this he did not mean that every squint should be photographed before and after operation but to take two small examples, more use could be made of photographs as records of growths, and, secondly, nothing could compare with colour photographs recording external conditions. He knew of no collection of colour photographic slides of external conditions in this Country such as he had seen in Brussels or in Calcutta; every eye department might well take a series of colour photographs of common eye diseases for teaching purposes.

His own particular interest was in fundus photography. Although fundus photography had reached a standard which made it of practical value, it still had some way to go before it achieved its full usefulness. One of the chief problems was exposure time. In the case of black-and-white photography an exposure of  $1/10$ th sec. gave good results, but in colour photography—especially as the standard of colour films had dropped since the war—it was necessary to give, so he understood, a  $\frac{1}{2}$  sec. exposure, and with the likelihood of movement of the eye of the patient, success was not obtained in more than 1 out of 3 or more exposures. This problem might be overcome by fitting to the fundus camera an electronic flash tube which gave an illumination of several thousand foot-candles. This would allow of an exposure of a few thousandths of a second.

Mr. Lister said that in selecting the photographs shown at the Meeting and, looking through the case-records attached to them, he was struck with the great possibilities which such photographs offered not only for teaching purposes but for the study of the ophthalmological aspects of systemic disease. He reminded the Section of the many varieties of retinal vascular change and of the value of having photographs of the fundus, taken at intervals in the course of a disease. The study of such a series might go a long way to solving some of the problems of the retinopathies and their causes. One wondered what Bright would have thought of it: the speaker then showed two illustrations of the fundus in Bright's disease. The first was a drawing made about 1860 soon after the ophthalmoscope was invented and the other was a recent photograph.

Mr. Fincham, speaking on the matter of exposures for fundus photograph which had been raised by Mr. Lister, said that with the use of the arc-lamp for monochrome photography an exposure of  $1/50$ th sec. did quite well. During his earlier remarks he had shown a Kodachrome which had received  $1/5$ th of a sec. Before the war an exposure of  $1/10$ th sec. for colour work could be given. But  $1/50$ th sec. for monochrome work was quite good.

Mr. B. W. Ryeröft said that he had one or two examples taken by a method which Mr. Lister had mentioned, namely, the electronic flash. This was used for external records and for the recording of an operation. Some difficulty was present in getting rid of the highlights. His subjects included a pre-operative view of a graft case with a central nebula; also a case of cantho-rhinostomy. He showed a series of pictures of the operation.

Mr. Lister wondered if the arc-lamp might not give unpleasant after-images. He himself used a filament lamp with which he could take several photographs, with only a very short after-image. He thought that the arc-lamp might be rather troublesome in this respect.

Mr. Fincham said that he had not found this to be so. He had used the arc on his colleagues and there had been no complaints from them. He had been interested in the suggestion as to the use of the light of the electronic flash for fundus photography. Unless one could form an optical image which was quite small he wondered whether this presented any advantage. It was a question of just masking it down for the size required. The great advantage of the arc was that it was a very small and intense source. The filament lamp embodied a special circular filament, and he wondered how one managed with the image when the light was from a fairly large source.

Mr. Lister said that, on the point mentioned by Mr. Fincham, methods of masking had been applied. It did not matter much about wasting the light so long as the exposure could be cut to a sufficiently short time.

# PROCEEDINGS

## OF THE

# ROYAL SOCIETY OF MEDICINE

Vol. XLII No. 7 July 1949

## CONTENTS

|                                                                                                                                              | Whole<br>Proceedings<br>Page |
|----------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|
| <b>Section of Surgery</b>                                                                                                                    |                              |
| <i>February 2, 1949</i>                                                                                                                      |                              |
| Persistent Painful States after Digital Nerve Injury.—R. P. JEPSON, M.B., B.Sc., F.R.C.S.                                                    | 459                          |
| Floss Silk Darn for Inguinal Hernia.—RODNEY MAINGOT, F.R.C.S.                                                                                | 465                          |
| An Operation for Hypospadias.—DENIS BROWNE, F.R.C.S.                                                                                         | 466                          |
| <i>March 23, 1949</i>                                                                                                                        |                              |
| The Use of Irradiation, Surgery and Hormones in Breast Cancer.—FRANK E. ADAIR, A.B., M.D., F.A.C.S., Hon.D.Sc., Hon.L.L.D.                   | 468                          |
| <b>Section of Experimental Medicine and Therapeutics</b>                                                                                     |                              |
| DISCUSSION: EVALUATION OF RENAL CLEARANCES                                                                                                   | 475                          |
| <b>Section of Orthopaedics</b>                                                                                                               |                              |
| The Treatment of Prostatic Secondary Deposits in Bone.—E. W. RICHES, M.C., M.S.                                                              | 481                          |
| Electrical Reactions of Muscle in Poliomyelitis.—IAN G. MACKENZIE, M.D.                                                                      | 488                          |
| <b>Section of Psychiatry</b>                                                                                                                 |                              |
| Sur les Explorations Pharmacodynamiques en Psychiatrie: Narco-analyse et Choc amphotaminique—Professor JEAN DELAY, M.D.                      | 491                          |
| <b>Section of Medicine</b>                                                                                                                   |                              |
| DISCUSSION ON PERIARTERITIS NODOSA                                                                                                           | 497                          |
| <b>Clinical Section</b>                                                                                                                      |                              |
| <i>February 11, 1949</i>                                                                                                                     |                              |
| Three Children Successfully Operated Upon for Congenital Atresia of the Oesophagus with Oesophago-tracheal Fistula.—R. H. FRANKLIN, F.R.C.S. | 507                          |
| Healed Miliary Tuberculosis of Liver and Spleen. Hepatomegaly, Splenomegaly.—G. KONSTAM, F.R.C.P.                                            | 512                          |
| <i>March 11, 1949</i>                                                                                                                        |                              |
| Four Cases of Intermittent Claudication.—PETER MARTIN, M.Chir.                                                                               | 513                          |
| Intermittent Claudication and Abdominal Aneurysm.—E. IDRIS JONES, M.D.                                                                       | 515                          |
| (1) Familial Haemorrhagic Telangiectasia (Rendu-Osler-Weber Disease)                                                                         | 515                          |
| (2) Non-familial Haemorrhagic Telangiectasia                                                                                                 | 516                          |
| W. A. BOURNE, M.D., and J. K. WAGSTAFF, M.R.C.P.                                                                                             |                              |
| <b>Section of Comparative Medicine</b>                                                                                                       |                              |
| <i>February 16, 1949</i>                                                                                                                     |                              |
| DISCUSSION: THE SIGNIFICANCE OF STRAIN DIFFERENCES IN VIRUS PROPHYLAXIS. [Abridged]                                                          | 517                          |
| <i>March 16, 1949</i>                                                                                                                        |                              |
| DISCUSSION: THE PHARMACOLOGICAL BASIS OF MODERN ANÆSTHESIA                                                                                   | 522                          |
| <b>Section of Otology</b>                                                                                                                    |                              |
| "Nerve" Deafness: Its Clinical Criteria, Old and New.—M. R. DIX, C. S. HALLPIKE and J. D. HOOD                                               | 527                          |
| The Causes of Perceptive Deafness.—R. R. SIMPSON, F.R.C.S.Ed.                                                                                | 536                          |
| <b>Section of Urology</b>                                                                                                                    |                              |
| <i>January 27, 1949</i>                                                                                                                      |                              |
| Pituitrin Therapy in Hydronephrosis.—J. G. YATES BELL, F.R.C.S.                                                                              | 541                          |
| The Operative Treatment of Urinary Incontinence in the Male.—G. M. LEWIS, F.R.C.S.                                                           | 547                          |

(Continued on next page)





NEW PRESENTATION  
25 mg. Glossettes.

REDUCTION IN PRICE  
of 5 mg. Glossettes.

# METHYLTESTOSTERONE

GLOSSO-STERANDRYL 25 mg. (ROUSSEL)

SUBLINGUAL ADMINISTRATION

NOW IN TWO STRENGTHS

5 mg. and 25 mg.

## ADVANTAGES OF THE 25 mg. GLOSSETTES

**Small Doses:** One 25 mg. Glossette per day, instead of five 5 mg. obviates the inconvenience of having to retain them in the mouth for a period five times as long.

**High Doses:** Until now, there has been no convenient method for the sublingual administration of high doses of male hormone. This is now possible using repeated daily administration of the 25 mg. Glossettes.

IN THE MALE: Hypogonitalism, Male climacteric, Senility.

IN THE FEMALE: Metrorrhagia, Premenopausal disorders.

5 mg. Glossettes: 20...12/9, 100...57/6, 500...266/-

25 mg. Glossettes: 10...28/-, 20...56/-, 100...252/- 250...610/-



ROUSSEL LABORATORIES LIMITED  
4 Golden Square, London, W.1 GERrard 3111/2

# PROCEEDINGS

## OF THE

# ROYAL SOCIETY OF MEDICINE

Vol. XLII No. 7 July 1949

## CONTENTS

Whole  
Proceedings  
Page

### Section of Surgery

*February 2, 1949*

Persistent Painful States after Digital Nerve Injury.—R. P. JEPSON, M.B., B.Sc., F.R.C.S. 459

Floss Silk Darn for Inguinal Hernia.—RODNEY MAINGOT, F.R.C.S. .. .. 465

An Operation for Hypospadias.—DENIS BROWNE, F.R.C.S. .. .. 466

*March 23, 1949*

The Use of Irradiation, Surgery and Hormones in Breast Cancer.—FRANK E. ADAIR, A.B., M.D., F.A.C.S., Hon.D.Sc., Hon.LL.D. .. .. 468

### Section of Experimental Medicine and Therapeutics

DISCUSSION: EVALUATION OF RENAL CLEARANCES .. .. 475

### Section of Orthopaedics

The Treatment of Prostatic Secondary Deposits in Bone.—E. W. RICHES, M.C., M.S... 481

Electrical Reactions of Muscle in Poliomyelitis.—IAN G. MACKENZIE, M.D. .. 488

### Section of Psychiatry

Sur les Explorations Pharmacodynamiques en Psychiatrie: Narco-analyse et Choc amphotaminique—Professor JEAN DELAY, M.D. .. .. 491

### Section of Medicine

DISCUSSION ON PERIARTERITIS NODOSA... .. 497

### Clinical Section

*February 11, 1949*

Three Children Successfully Operated Upon for Congenital Atresia of the Œsophagus with Œsophago-tracheal Fistula.—R. H. FRANKLIN, F.R.C.S. .. .. 507

Healed Military Tuberculosis of Liver and Spleen. Hepatomegaly, Splenomegaly.—G. KONSTAM, F.R.C.P. .. .. 512

*March 11, 1949*

Four Cases of Intermittent Claudication.—PETER MARTIN, M.Chir. .. .. 513

Intermittent Claudication and Abdominal Aneurysm.—E. IDRIS JONES, M.D. .. 515

(1) Familial Hemorrhagic Telangiectasia (Rendu-Osler-Weber Disease) .. .. 515

(2) Non-familial Hemorrhagic Telangiectasia .. .. 516

W. A. BOURNE, M.D., and J. K. WAGSTAFF, M.R.C.P.

### Section of Comparative Medicine

*February 16, 1949*

DISCUSSION: THE SIGNIFICANCE OF STRAIN DIFFERENCES IN VIRUS PROPHYLAXIS. [Abridged] 517

*March 16, 1949*

DISCUSSION: THE PHARMACOLOGICAL BASIS OF MODERN ANÆSTHESIA .. .. 522

### Section of Otology

"Nerve" Deafness: Its Clinical Criteria, Old and New.—M. R. DIX, C. S. HALLPIKE and J. D. HOOD .. .. 527

The Causes of Perceptive Deafness.—R. R. SIMPSON, F.R.C.S.Ed. .. .. 536

### Section of Urology

*January 27, 1949*

Pituitrin Therapy in Hydronephrosis.—J. G. YATES BELL, F.R.C.S. .. .. 541

The Operative Treatment of Urinary Incontinence in the Male.—G. M. LEWIS, F.R.C.S. 547

(Continued on next page)



NEW PRESENTATION  
25 mg. Glossettes.

REDUCTION IN PRICE  
of 5 mg. Glossettes.

# METHYLTESTOSTERONE

GLOSSO-STERANDRYL 25 mg. (ROUSSEL)

SUBLINGUAL ADMINISTRATION

NOW IN TWO STRENGTHS

5 mg. and 25 mg.

## ADVANTAGES OF THE 25 mg. GLOSSETTES

**Small Doses:** One 25 mg. Glossette per day, instead of five 5 mg. obviates the inconvenience of having to retain them in the mouth for a period five times as long.

**High Doses:** Until now, there has been no convenient method for the sublingual administration of high doses of male hormone. This is now possible using repeated daily administration of the 25 mg. Glossettes.

IN THE MALE: Hypogonitalism, Male climacteric, Senility.

IN THE FEMALE: Metrorrhagia, Premenopausal disorders.

5 mg. Glossettes: 20...12/9, 100...57/6, 500...266/-

25 mg. Glossettes: 10...28/-, 20...56/-, 100...252/- 250...610/-



ROUSSEL LABORATORIES LIMITED  
4 Golden Square, London, W.1 GERRARD 3111/2

## Section of Surgery

President—JULIAN TAYLOR, C.B.E., M.S., F.R.C.S.

[February 2, 1949]

### Persistent Painful States after Digital Nerve Injury

By R. P. JEPSON, M.B., B.Sc., F.R.C.S.

*The Surgical Professorial Unit, The Royal Infirmary, Manchester*

#### Material Studied

FOLLOWING injury to peripheral nerves, persistent and often incapacitating pains may arise, which vary greatly in their severity, quality, distribution and association with other phenomena. 16 cases of such persistent painful states are reviewed in this paper. All had lesions of the digital nerves, incurred through surgical incisions for sepsis, amputation or incisional trauma. No lesions to more proximal peripheral nerves have been included in this series. Digital nerve injuries associated with fractures, dislocations or gross blunt trauma have been excluded (Table I).

TABLE I.—SUMMARY OF CASE HISTORIES

| Case               | Age | Mechanism of injury                | Sepsis | Major presenting symptoms          | Length of history in years |
|--------------------|-----|------------------------------------|--------|------------------------------------|----------------------------|
| 1 J. McD. (M.)     | 33  | Laceration .. ..                   | +      | Burning .. ..                      | 4                          |
| 2 H. S. (M.)       | 48  | Incis.—steel splinter .. ..        | +      | Cold-ache .. ..                    | 1                          |
| 3 E. S. (F.)       | 42  | Incis.—felon .. ..                 | +      | Cold-ache .. ..                    | 2                          |
| 4 J. L. (M.)       | 30  | Amput.—stiff painless finger .. .. | —      | Cold-ache .. ..                    | 9                          |
| 5 A. W. (M.)       | 30  | Laceration .. ..                   | —      | Hyperæsthesia .. ..                | 2                          |
| 6 J. J. B. (M.)    | 40  | Incis.—felon .. ..                 | +      | Cold-ache .. ..                    | 4                          |
| 7 J. F. B. L. (M.) | 39  | Excis.—neuroma .. ..               | —      | Hyperæsthesia .. ..                | 5                          |
| 8 J. G. (M.)       | 37  | Incis.—felon .. ..                 | +      | Cold-ache "Pins and needles" .. .. | 4                          |
| 9 D. C. (F.)       | 39  | Incis.—felon .. ..                 | +      | Cold-ache .. ..                    | 1                          |
| 10 J. B. (M.)      | 31  | Incis.—septic lacer. .. ..         | +      | Cold-ache .. ..                    | 1                          |
| 11 J. F. (M.)      | 37  | Incis.—septic lacer. .. ..         | +      | Tactile paræsthesiæ .. ..          | 3/12                       |
| 12 I. W. (F.)      | 30  | Incis.—felon .. ..                 | +      | Hyperæsthesia .. ..                | 3/12                       |
| 13 B. W. (F.)      | 43  | Incis.—felon .. ..                 | +      | Cold-ache .. ..                    | 3/12                       |
| 14 C. L. (F.)      | 32  | Incis.—felon .. ..                 | +      | Tactile paræsthesiæ .. ..          | 3/12                       |
| 15 B. A. (M.)      | 40  | Incis.—felon .. ..                 | +      | Tactile paræsthesiæ .. ..          | 3/12                       |
| 16 S. S. (F.)      | 50  | Incis.—felon .. ..                 | +      | Cold-ache .. ..                    | 6/12                       |

In all 16 cases there was evidence of digital nerve damage as shown by hypo-æsthesia or hypo-algesia although in the majority of cases the section was either incomplete or concerned with a terminal pulp branch alone. Sepsis had been present in 13 of the cases. 10 cases occurred in men and 6 in females, their ages ranging from 30 to 50 years. In 7 cases the digit involved was the thumb, in 7 the forefinger and in 2 the middle finger.

An attempt has been made to analyse the pains, particularly their quality, their threshold of sensitivity and the factors modifying their intensity.

A description is given below of some of the characteristic clinical histories which were recorded in this series of cases. For the sake of brevity, the case-histories of all 16 patients are not given, but may be assumed to resemble with modification that quoted at length. A summary of the whole group is presented in Table I.

Section of Urology (*continued*)

March 24, 1949

Vesical Diverticula. [*Abridged*].—HOWARD G. HANLEY, M.D., F.R.C.S. .. .. 548

April 28, 1949

List of Cases and Specimens Shown .. .. . 556

## Section of Pædiatrics

October 22, 1948, *concluded*

Polyostotic Fibrous Dysplasia.—J. R. D. WEBB, O.B.E., M.R.C.P., D.P.H., D.C.H. .. 557

January 28, 1949

Nephrocalcinosis in Infancy.—B. W. POWELL, M.R.C.P. (for P. R. EVANS, M.D.) 559

Ollier's Disease (Dyschondroplasia).—ALEX RUSSELL, O.B.E., M.R.C.P. (for C. T. POTTER, M.D.) 559

Hepatic Cirrhosis Following Neonatal Jaundice (Specimen).—E. HINDEN, M.D. 560

Green Teeth Following Icterus Gravis Neonatorum.—C. W. KESSON, M.D. (for CHARLES PINCKNEY, F.R.C.P.) 561

Spasmus Nutans.—JOHN BURKINSHAW, M.B., M.R.C.P. (for C. W. KESSON, M.D.) .. 562

Hemihypertrophy. ? Hæmangioma.—M. W. ARTHURTON, M.R.C.P. (for DAVID LEVI, M.S.) .. .. . 562

(N.B.—The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.)

**Copyright:** The Society holds the copyright of all matter accepted for publication in the *Proceedings*. Requests for subsequent publication elsewhere should be made to the Honorary Editors. All papers, &c., presented at meetings (other than those which have been previously published) are held to be subject to the Society's copyright until a decision in regard to their publication has been made.

**Digests:** Requests for permission to make Digests from the *Proceedings* should be addressed to the Honorary Editors.

All communications concerning Editorial Business should be addressed to  
THE HONORARY EDITORS, 1, WIMPOLE STREET, LONDON, W.1

Applications for advertisement space in the "*Proceedings*" should be made to the Society's official advertising agents, Messrs. C. Mitchell & Co. Ltd., Mitchell House, 1 and 2, Snow Hill, London, E.C.1.

Copies of the whole *Proceedings* may be purchased through any bookseller. Prices are as follows:—

Single copies .. .. . 10s. 6d. each, post free.

Annual subscription, covering 12 monthly issues and annual index .. .. . £6 6s. 0d.

Reprints of Sectional parts may be obtained direct from the Society. Prices are as follows:—

Single copies .. .. . 3s. 6d. each, post free.

Annual subscription .. .. . 15s. 0d.

Fellows and Members of the Royal Society of Medicine are asked to apply direct to the Society for any copies of the *Proceedings* they may require, whether whole or Sectional, in addition to those they receive *gratis*. Prices are as follows:—

Whole *Proceedings*:

Single copies .. .. . 7s. 6d. each, post free.

Complete volume (12 monthly issues and annual index) .. .. . £5 0s. 0d.

Sectional *Proceedings*:

Single copies .. .. . 3s. 0d. each, post free.

Annual subscription .. .. . 10s. 0d.



## Prolonged effective action ...

has been achieved by the introduction of Procaine Penicillin Oily Injection A&H, a suspension of procaine penicillin-G with 2 per cent. aluminium stearate in sterile arachis oil. Each c.c. contains 300,000 units of penicillin and the equivalent of 120 mg. of procaine. The aluminium stearate, together with the sparing solubility of the procaine penicillin, retards the liberation of penicillin into the blood stream, thus prolonging the therapeutic action.

Procaine Penicillin Oily Injection A&H is administered, with little or no pain, by intramuscular injection. Generally, a single injection of 1 c.c. daily is sufficient.

Available in vials of 10 c.c.

## PROCAINE PENICILLIN OILY INJECTION A&H

ALLEN & HANBURYS LTD LONDON E 2  
TELEPHONE BISHOPSQATE 3201 (17 LINES) TELEGRAMS "GREENBURYS BETH LONDON"

### Spontaneous Pain

(a) *Deep-ache*.—By far the commonest spontaneous pain in this series is the deep ache. It was the presenting symptom in most cases and was experienced by 14 out of the 16 patients. (Kellgren, McGowan and Hughes found 9 cases out of 32 cases of painful digital nerve injuries.) It had the quality of a deep pain and was referred in the milder states to the region of the nerve damage, tending to spread with increasing severity distally into the "phantom" when present, and proximally up the limb. It does not follow a peripheral nerve distribution and its reference is probably segmental. It is felt "deeply" in the limb and may be compared clinically to the pain arising from compression of the thenar muscles. Commonly associated with the spontaneous deep-ache are hyperalgesia, vasomotor changes and motor disturbances.

The patient himself has usually noticed that the ache is aggravated by any factor cooling the part, and to a lesser degree by pressure, palpation or movement of the affected area and digit. Relief is sought through warmth and, in its more severe manifestations, the pain may compel the patient to sit with the hand exposed to a fire or radiator or immersed in hot water. Its nagging, gnawing persistence soon undermines the patient's stability and he becomes irritable and unco-operative. Sleeplessness arises and a deterioration in the physical and mental wellbeing is soon evident.

As described by Kellgren, McGowan and Hughes this deep-ache following nerve section is closely linked with the temperature of the part and is most dramatically influenced by cold. It may well be described as a "cold-ache". Should both the normal and affected limb be immersed in water of a controlled temperature, it is found that the injured finger begins to ache well above the normal temperature threshold for pain (cold-pain threshold), and if the temperature is lowered the ache so increases that it may be impossible to keep the finger immersed, although the normal hand is as yet unaffected. The temperature sensitivity of the affected digit is exceedingly finely adjusted. Thus patient S. S. could with the affected thumb (left) distinguish  $\frac{1}{2}^{\circ}\text{C}$ . difference in water temperature,  $21\frac{1}{2}^{\circ}\text{C}$ . gave rise to ache, whilst  $22^{\circ}\text{C}$ . was comfortable after five minutes' immersion.

|             | C. $25^{\circ}$ | $22^{\circ}$ | $21^{\circ}$ | $15^{\circ}$ |
|-------------|-----------------|--------------|--------------|--------------|
| R. thumb .. | 0               | 0            | 0            | $\pm$        |
| L. thumb .. | 0               | 0            | +            | +++          |

*Patient S. S.—Showing pain-temperature correlation in normal and affected thumbs.*

Blocking the sympathetic supply to the digit by a stellate ganglion novocain injection, or by tetra-ethyl-ammonium bromide (T.E.A.B.) will relieve the pain only if the limb temperature is allowed to rise subsequent to the vasodilatation. The pain returns if the limb is immersed in water below the original pre-injection threshold for spontaneous pain. This was true in Case E. S. six months after a stellate ganglionectomy. Although she now complained of no spontaneous pain (resting finger temperature  $29^{\circ}\text{C}$ . in R.T. of  $22^{\circ}\text{C}$ .) cooling the hand to  $22^{\circ}\text{C}$ . brought on severe cold-ache.

Blocking the perivascular plexus by novocain infiltration around the radial artery at the wrist in case of the thumb did not influence the pain. Increasing the venous congestion to the limb by a sphygmomanometer cuff at 60 mm. Hg pressure, or ischaemia by maintaining the cuff above systolic pressure for ten minutes, did not affect the pain if the finger temperature was controlled. Ischaemia, through allowing quicker adjustment between tissue and environment temperature, may accelerate pain when the finger is immersed in water below the threshold temperature.

The deep-ache was always accompanied by arterial spasm usually to a marked degree, resulting in a persistently low hand, finger and sometimes arm temperature. This approximation of the abnormally low limb temperature to the cold-pain threshold, results in the early onset of pain when the hand is exposed to a cooling environment. Should the limb temperature be below the cold-pain threshold at an average room temperature, as in several cases in this series, then the patient's life is a constant search for a warm environment and he takes great care to keep the hand covered and unexposed.

Another constant feature of the patient with a "deep-ache" is the marked hyperalgesia of the deep tissues of the affected limb and shoulder girdle. This will be discussed in detail later in the paper.

A pain of similar deep quality and distribution is experienced by some patients on movement of the hand or fingers or by touching the scar region. This is apparently a "mechanical" stimulation of abnormal nerve fibres or endings, which have a much lowered threshold. It is uninfluenced by interruption of the sympathetic, circulatory or temperature changes, though relieved by a novocain block of the somatic nerve to the scar region.

CASE 3.—E. S., female, housewife.

A pulp-space infection of the right middle finger was opened on 17.12.46 by a "hockey-stick" incision. It quickly healed and she was discharged two weeks later. The patient returned on 13.1.47 complaining of a severe ache in the finger which was aggravated by cold. The scar was extremely sensitive to light touch and on gripping anything with the incised finger a "pins and needles" radiated proximally to the metacarpo-phalangeal joint. The right arm was "weaker" than before and the hand whilst holding objects would relax suddenly and involuntarily. She had broken a great deal of crockery because of this. Occasionally the whole arm would twitch involuntarily. The affected hand always felt cold.

On examination the troublesome finger was held in a semi-flexed position, was blue and 5° to 6° C. colder than the corresponding finger on the left hand. The skin of the finger had lost its creases, and was shiny, tapering. Proximally the finger was beaded with sweat and the hair growth was exceptionally profuse over the proximal phalanx. She was unable to open and close the right hand quickly, or flex the third finger more than 30 to 40 degrees, and this only with a great deal of concentrated effort. The whole of the right arm was 2° to 3° cooler than the left and its oscillometric readings over the upper and fore-arm decreased by nearly 50%. The pulp scar was extremely sensitive to light stroking with cotton-wool and blunt pressure was greatly resented as "pins and needles" radiated up to the metacarpo-phalangeal joint. Distal to the scar was an anesthetic patch showing that the digital nerve had been at least partially divided.

On 2.10.47 the finger was amputated at the proximal interphalangeal joint. This abolished the persistent deep-ache for a few weeks but all the subjective and objective phenomena had returned by 3.11.47. On 16.12.47 the finger was amputated at the metacarpo-phalangeal joint. Again after a painless interval of a few weeks all the phenomena returned. On 8.7.48 a stellate ganglionectomy was performed resulting in the disappearance of the vasomotor phenomena, hyperaesthesia and the ache. Except for a little "tingling" on pressure over the scar, the hand can be used freely.

### Analysis of Painful States

Many different pain syndromes have been described after peripheral nerve injury and a wealth of descriptive titles applied to them. (Some are shown in Table II.) These are mostly

TABLE II.—DESCRIPTIVE TITLES GIVEN TO PAINS FOLLOWING PERIPHERAL NERVE LESIONS

| Name                                      | Reference                                      |
|-------------------------------------------|------------------------------------------------|
| (i) Causalgia                             | Mitchell, S. W. (1872)                         |
| (ii) Minor causalgia                      | Homans, J. (1940)                              |
| (iii) Post-traumatic pain                 | Doupe, J., Cullen, C. R., Chance, G. Q. (1944) |
| (iv) Causalgic syndrome                   |                                                |
| (v) Dystrophic pain                       |                                                |
| (vi) Sympathetic nerve system pains       | Mahorner, H. (1944)                            |
| (vii) Sympathalgia                        |                                                |
| (viii) Post-traumatic dystrophy           | Miller, D., and de Takats, G. (1942)           |
| (ix) Reflex dystrophy                     | de Takats, G. (1937)                           |
| (x) Reflex sympathetic dystrophy          | Evan, J. A. (1946)                             |
| (xi) Traumatic neuralgia                  | Bingham, J. A. W. (1948)                       |
| (xii) Trophoneurosis                      | Vulpian (cit.) Adams-Ray, J. (1944)            |
| (xiii) Post-traumatic ascending neuralgia | Leriche (1937)                                 |

defined from one outstanding symptom or by the author's conception of the pathogenesis of the pains and allied phenomena. They may be misleading especially if unqualified by clinical or physiological data.

In this paper, for the purposes of clinical analysis, two groups of abnormal pain sensation have been distinguished. First that arising "spontaneously" and secondly that produced by a mechanical stimulus. These again are subdivided into "cutaneous" and "deep" pain.

On reviewing this series therefore the following descriptive classification is tentatively suggested (Table III). Reasons for such classification will it is hoped become apparent in the text.

TABLE III

Cutaneous

Deep

|                        |                                                                             |                                                    |
|------------------------|-----------------------------------------------------------------------------|----------------------------------------------------|
| Spontaneous            | .. .. Burning. (Syn. Causalgia)                                             | Ache                                               |
|                        | Abnormal sensations not amounting to pain. ("pins and needles"; pricking)   | (Syn. throbbing)                                   |
| Mechanical Stimulation | .. Lowered threshold to Frey's hair. (Syn. Hyperaesthesia)                  | Lowered threshold to pressure. (Syn. Hyperalgesia) |
|                        | Abnormal sensory response not amounting to pain. (Syn. Tactile paresthesia) |                                                    |

### Spontaneous Pain

(a) *Deep-ache*.—By far the commonest spontaneous pain in this series is the deep ache. It was the presenting symptom in most cases and was experienced by 14 out of the 16 patients. (Kellgren, McGowan and Hughes found 9 cases out of 32 cases of painful digital nerve injuries.) It had the quality of a deep pain and was referred in the milder states to the region of the nerve damage, tending to spread with increasing severity distally into the "phantom" when present, and proximally up the limb. It does not follow a peripheral nerve distribution and its reference is probably segmental. It is felt "deeply" in the limb and may be compared clinically to the pain arising from compression of the thenar muscles. Commonly associated with the spontaneous deep-ache are hyperalgesia, vasomotor changes and motor disturbances.

The patient himself has usually noticed that the ache is aggravated by any factor cooling the part, and to a lesser degree by pressure, scar palpation or movement of the affected area and digit. Relief is sought through warmth and, in its more severe manifestations, the pain may compel the patient to sit with the hand exposed to a fire or radiator or immersed in hot water. Its nagging, gnawing persistence soon undermines the patient's stability and he becomes irritable and unco-operative. Sleeplessness arises and a deterioration in the physical and mental wellbeing is soon evident.

As described by Kellgren, McGowan and Hughes this deep-ache following nerve section is closely linked with the temperature of the part and is most dramatically influenced by cold. It may well be described as a "cold-ache". Should both the normal and affected limb be immersed in water of a controlled temperature, it is found that the injured finger begins to ache well above the normal temperature threshold for pain (cold-pain threshold), and if the temperature is lowered the ache so increases that it may be impossible to keep the finger immersed, although the normal hand is as yet unaffected. The temperature sensitivity of the affected digit is exceedingly finely adjusted. Thus patient S. S. could with the affected thumb (left) distinguish  $\frac{1}{2}^{\circ}\text{C}$ . difference in water temperature,  $21\frac{1}{2}^{\circ}\text{C}$ . gave rise to ache, whilst  $22^{\circ}\text{C}$ . was comfortable after five minutes' immersion.

|             | C. $25^{\circ}$ | $22^{\circ}$ | $21^{\circ}$ | $15^{\circ}$ |
|-------------|-----------------|--------------|--------------|--------------|
| R. thumb .. | 0               | 0            | 0            | $\pm$        |
| L. thumb .. | 0               | 0            | +            | +++          |

*Patient S. S.—Showing pain-temperature correlation in normal and affected thumbs.*

Blocking the sympathetic supply to the digit by a stellate ganglion novocain injection, or by tetra-ethyl-ammonium bromide (T.E.A.B.) will relieve the pain only if the limb temperature is allowed to rise subsequent to the vasodilatation. The pain returns if the limb is immersed in water below the original pre-injection threshold for spontaneous pain. This was true in Case E. S. six months after a stellate ganglionectomy. Although she now complained of no spontaneous pain (resting finger temperature  $29^{\circ}\text{C}$ . in R.T. of  $22^{\circ}\text{C}$ .) cooling the hand to  $22^{\circ}\text{C}$ . brought on severe cold-ache.

Blocking the perivascular plexus by novocain infiltration around the radial artery at the wrist in case of the thumb did not influence the pain. Increasing the venous congestion to the limb by a sphygmomanometer cuff at 60 mm. Hg pressure, or ischaemia by maintaining the cuff above systolic pressure for ten minutes, did not affect the pain if the finger temperature was controlled. Ischaemia, through allowing quicker adjustment between tissue and environment temperature, may accelerate pain when the finger is immersed in water below the threshold temperature.

The deep-ache was always accompanied by arterial spasm usually to a marked degree, resulting in a persistently low hand, finger and sometimes arm temperature. This approximation of the abnormally low limb temperature to the cold-pain threshold, results in the early onset of pain when the hand is exposed to a cooling environment. Should the limb temperature be below the cold-pain threshold at an average room temperature, as in several cases in this series, then the patient's life is a constant search for a warm environment and he takes great care to keep the hand covered and unexposed.

Another constant feature of the patient with a "deep-ache" is the marked hyperalgesia of the deep tissues of the affected limb and shoulder girdle. This will be discussed in detail later in the paper.

A pain of similar deep quality and distribution is experienced by some patients on movement of the hand or fingers or by touching the scar region. This is apparently a "mechanical" stimulation of abnormal nerve fibres or endings, which have a much lowered threshold. It is uninfluenced by interruption of the sympathetic, circulatory or temperature changes, though relieved by a novocain block of the somatic nerve to the scar region.



(b) *Burning pain*.—Only one case (J. McD.) complained of this pain. Although it is often stated that a true causalgia is not seen after digital nerve injuries, there is no doubt that this man exhibited the classical "constant burning pain" with paroxysmal exacerbations as described in Weir Mitchell's original description and re-emphasized recently by Nathan and Boyd. Except for short periods following surgical intervention it had been present since the first injury. It was constantly present, markedly intensified by a definite temperature range and completely relieved by a stellate ganglion novocain block. The limb in contrast to the other cases in the series was warmer than the normal side. The scar region was exquisitely hyperæsthetic.

The site of origin of the causalgic pain appears to be, as for the deep-ache, at the point of nerve division. It is probably conducted via the somatic nerves (Nathan). Thus in this case it was abolished by novocain injections in the region of the scar and by digital or more proximal somatic nerve blocks. In contrast, however, to the cold-ache described previously, this burning pain is dramatically removed by a block of the sympathetic nerves to the part. It was found by placing the affected hand in water baths of controlled temperature that the pain was least severe between a range of about 28°–35° C. Any temperature outside the range increased the pain particularly when it was above 35° C. With the hand placed in water of 37° C., when the burning pain was intense, a stellate ganglion novocain block was performed. This could not increase the local blood flow to the limb as full vasodilatation had already been obtained through local heat (room temperature 24° C.). Nevertheless the burning pain disappeared immediately following the injection, the patient saying with delight that this was the first time that the pain had been taken away for years. A similar experiment, using T.E.A.B. in place of direct ganglion injection, also relieved the pain. Perivascular novocain infiltration of the radial artery at the wrist did not affect the pain.

*Abnormal sensations not amounting to pain*.—These are bizarre sensations described by the patient as throbbing, pricking, "pins and needles", &c. Usually they are minor discomforts localized to the injured finger and not amounting to real pain. They are only brought into prominence when the severer pains such as the burning and deep-ache have been removed.

#### *Pain Due to Mechanical Stimulation*

(c) *Lowered threshold to Frey's hair (hyperæsthesia)*.—It was found in 9 cases in this series that light mechanical stimulation to the region of the scar and its surround by a Frey's hair or fine nylon filament caused a characteristic response. The patient finds it difficult to convey the quality of the sensation, but states that it is extremely unpleasant, explosive in its suddenness, and associated with an involuntary withdrawal of the part from the stimulus. When this phenomenon was present the patient was unable to use the finger for any task, however light and delicate it might be, and he took extreme precautions to protect the skin from any contact. For brevity we have called this type of response to light mechanical stimulation, hyperæsthesia.

The hyperæsthetic area was always most pronounced in the region of the scar and immediate surround, though the whole limb may show some changes. It was often confusedly mixed distal to the lesion with patchy hypo-æsthetic areas. It was, with the exception of one individual (A. W.), always associated with other post-traumatic pains.

The hyperæsthesia was uninfluenced by immersing the hand in water 15°–45° C., except that occasionally the patient thought it was lessened slightly in the colder water. Venous congestion or ischæmia of the arm for ten minutes did not influence the sensitivity. It is thus clearly distinct from the state of "erythralgia" described by Lewis and Harpman. In 3 out of the 7 cases blocking of the sympathetic nerve supply to the arm abolished the hyperæsthesia. In only 1 case (A. W.) was this permanent; in the remaining 2 patients it returned to the pre-injection state within twenty-four hours.

A novocain block of the scar region or the afferent somatic nerve supply temporarily removed the tactile hypersensitivity. Why sympathetic interruption abolished the hyper-æsthesia in some and not in others was not understood.

(d) *Lowered threshold to pressure (deep hyperalgesia)*.—This was present to a marked degree in 7 patients though present to some extent in all who complained of a cold-ache. It was tested by a blunt-nosed (1 sq. cm.) spring algometer measuring graded pressure up to a maximum of 5 kilograms. Clinically it can be plotted by thumb pressure. It is usually not feasible to test the deep sensitivity in the region of the scar but pressure on the rest of the hand, forearm, upper arm and shoulder-girdle musculature can be tolerated by the patient and compared with the normal arm. The pain produced by such blunt pressure arises in the deep tissues especially deep fascia, muscle, periosteum, and a fraction of the pressure necessary to produce deep pain in the normal arm, will cause an unbearable ache on the side of the

finger lesion. Not only is the threshold to pain lower, but the ensuing ache persists longer than that of the normal side. In one case (H. S.) a sphygmomanometer cuff pumped to 220 mm. Hg pressure could not be tolerated for more than two minutes on the upper arm. This patient had noticed himself that any pressure on the arm caused aching and he was unable to rest his arm on the table, or should he lie on the affected arm at night he was awakened by pain. Except for one case (H. S.) a pronounced deep hyperalgesia was always accompanied by a spontaneous cold-ache. The deep hyperalgesia was not affected by sympathetic interruption or local block to the region of the sectioned nerve. 2 cases were followed for six months after a stellate ganglionectomy for a cold-ache, and in these the deep hyperalgesia to mechanical stimuli remained unchanged. This is in agreement with the findings of Kellgren, McGowan and Hughes (1948).

(e) *Abnormal sensory response not amounting to pain: Tactile paræsthesiæ.*—When blunt pressure is applied to the region of a regenerating nerve, a tingling pain is experienced, which has a limited reference up the finger and occasionally higher up the limb. This is a minor discomfort and, if not accompanied by other pains, can be tolerated without complaint. No detailed investigations were made on this pain.

### *Associated Phenomena*

Most post-traumatic nerve pains have associated phenomena. Amongst those seen in this series were: arterial and venous spasm, arterial dilatation, involuntary motor activity, wasting of soft tissues, osteoporosis, hypo- or hyperhidrosis, hypo- or hypertrichosis, nail changes, œdema of fingers and hand. An excellent historical review of these phenomena has been made by Adams-Ray.

These changes in limb nutrition and vascular supply are not present in the same degree or proportions in each case. Nor is the intensity or type of pain in direct relationship to their presence or absence.

### *Genesis of the Pains*

In the first place all the abnormal pain sensation would seem to have begun in the sensory disturbance arising in the region of the sectioned nerve. Later a more widespread sensory defect occurs, causing deep hyperalgesia, and diffuse hyperæsthesia over a much wider distribution, which may now be unaffected by new conditions in the original nerve lesion. What happens at the site of the sectioned nerve to originate a painful state has been the subject of many hypotheses. Wilfred Trotter's suggestion has recently received support from the histological inquiries of Weddell and his co-workers. This suggests that there is an outgrowth of abnormal neurofibrils from the proximal end of the cut nerve into the deep tissues and the skin. Due perhaps to the "non-insulation" of these fibres, their abnormal anatomical pattern or linkage with abnormal end-organs, they are "fired" by stimuli which normally would not be adequate. These stimuli may be metabolic, thermal or mechanical in origin. In some cases artificial synapses may be established between the sympathetic efferents and somatic afferents. Doupe, Cullen and Chance have put forward the latter suggestion to explain the causalgic syndrome. Vasospasm is without doubt a frequent accompaniment of some painful states. Its relief, however, does not directly affect the pain, nor is its degree proportionate to the severity of the pain. The psychological background of the patients described in this series was investigated. All proved to have been stable personalities previous to the injury and many have suffered previous to the present accident far more severe trauma. However nervous and anxious the patient was at the time of the examination, it was felt that this was the result of the pain rather than its cause.

Although the majority of the cases in the series had infected wounds during their healing, 3 patients had at no time shown evidence of clinical sepsis. Infection at the site of nerve injury may influence abnormal neural regeneration, although there is as yet no evidence for this. Leriche states that an "ascending neuritis" has never been demonstrated as a clinical entity and until histological and bacteriological proof is available it would seem that nothing is to be gained by this conception.

### TREATMENT

The following treatments had been used in one or more of the cases in this series of post-traumatic pains, usually prior to arrival at the clinic.

(a) Conservative measures of rest, splintage, short-wave diathermy, physiotherapy, reassurance and settlement of compensation.

(b) Excision of neuroma.

(c) Excision of wedge of tissue to include skin, nerve, connective tissue and periosteum at site of lesion.

JULY—SURG. 2

In our hernia work we owe much to the use of penicillin, as serious sepsis in the wound and sinus formation have been eliminated.

This operation is applicable to all types of inguinal hernia—direct, indirect and recurrent—except the small congenital hernia of children and young adults with good muscular and fascial supports where simple herniotomy, followed by repair of the internal ring, is the procedure of choice.

I set no age-limit on my cases for hernia surgery, and only refuse those in which there are definite contra-indications such as pulmonary tuberculosis, &c.

The important steps of the operation are:

- (1) Crease incision, as it heals well and the scar is flexible and almost invisible.
- (2) Stripping the cremaster muscle from the cord and removing an indirect sac after transfixion and ligation of the neck.
- (3) Suturing the cremaster and transversalis fascia (from the point where the cord issues from the internal ring to pubic spine) to Poupart's ligament.
- (4) The insertion of the floss silk darn from the pubic tubercle to the point where the cord issues from the internal ring and then back again to the symphysis. The first row is inserted along Poupart's ligament and the conjoint tendon, whilst the returning layer is introduced with a wider traverse—rectus sheath to Poupart's ligament.
- (5) Approximation of the cut edges of the external oblique aponeurosis *behind* the cord.
- (6) Ensuring that there is no gap or weak spot where the cord issues through the newly constructed combined rings.

Floss silk is preferred to nylon, fascia lata, kangaroo tendon, stainless steel wire, tantalum wire, stout twisted silk, and other materials, because it is a beautifully soft material consisting of the individual fibrils of natural silk, offering a perfectly pliable framework for the subsequent growth of fibroblasts.

[The precise method of introducing the lattice or darn repair was then shown on the film.]

The silk darn becomes incorporated into the tissues and stimulates the formation of a firm, strong but flexible barrier of fibrous tissue, making the area as strong as the tissues into which the lattice extends.

As the repair—firm but not too tight—is sound in practice and in principle, we allow our patients out of bed on the day following the operation and they are discharged from hospital on the eighth day.

They return to light duty in six weeks and to routine work in two months.

In our hands, the sepsis rate is less than 1%, whilst the recurrence rate has never exceeded 3%.

Our highest recurrence rate was in those cases operated on both sides at the same time; now, we allow an interval of ten days between the operations and this factor alone has done much to improve our results.

## An Operation for Hypospadias

By DENIS BROWNE, F.R.C.S.

*Surgeon to The Hospital for Sick Children*

THERE are four simple and obvious requirements for an operation for hypospadias:

- (1) It should be applicable to all degrees of the deformity.
- (2) It should be capable of regular completion before the age at which it becomes important to the child to pass urine in the normal masculine manner. That is the age of 5 years, at which schooling in this country is usually begun.
- (3) It should produce a urethra equivalent in diameter and elasticity with the normal.
- (4) It should be within the power of any competent surgeon, and not need either exceptional skill or exceptional fortune for success.

Without going at length into the immense number of procedures advocated for this condition, it will be evident that no single one of them fulfils the first, second, or fourth requirements, and the various methods of forming a urethra by skin grafts do not fulfil the third.

The method here described I believe to fulfil them all. It turns upon the curious fact that the skin of the penis never forms keloid, nor does the subcutaneous tissue thicken and contract following granulation and healing as is the rule elsewhere in the body. Because of this, if a strap of skin is buried along the line where a new urethra is desired it will automatically form itself into a tube without stricture in diameter nor contraction in length.

Similarly the relaxation necessary to enable this strip to be buried can be provided by a simple incision upon the other side, the dorsum, of the penis; the raw surface being left to epithelialize itself.

Urine must be diverted during the process of healing; and this is done by perineal drainage through a Malecot catheter.

The skin of the penis, although it heals very well, is extremely thin and fragile, and will not stand the tension of ordinary sutures. In consequence I have found it best to use what I call the "double stop" suture to hold the lateral flaps together. This "double stop" consists of one structure to put pressure upon the skin, and another to hold this to the suture. The second stop consists of a small segment of soft aluminium tubing, which can be crushed upon the stitch itself, and the first, or skin stop, varies in size and shape according to the region of the body. In the penis a glass bead  $\frac{1}{4}$  in. in diameter is very satisfactory.

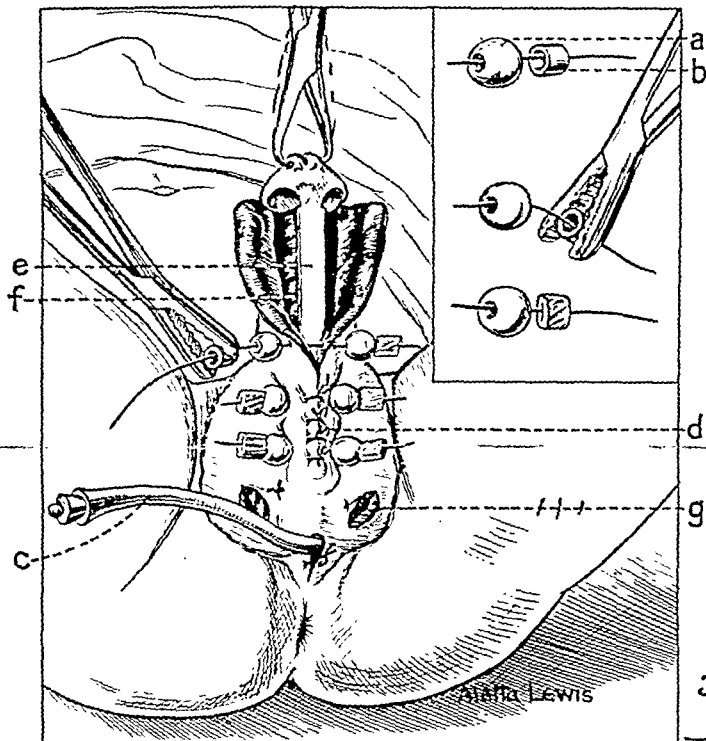


FIG. 1.—a. Glass bead. b. Aluminium cylinder. c. Malecot catheter in perineal urethra. d. Fine catgut sutures joining skin edges. e. Strap of skin to be buried to form the new urethra. f. Raw surfaces of lateral flaps of skin of penis. g. Incisions in scrotum to allow exit of serum.

#### STEPS OF THE OPERATION

##### I. Primary freeing of the chordee of penis, preferably at 18 months of age.

A transverse cut is made just proximal to the glans across the ventral surface of the penis, continued laterally into the prepuce on either side. All contracted tissues down to the corpora cavernosa are divided and allowed to slide towards the base of the penis. The transverse skin incision is then sewn up longitudinally with fine catgut and an incision made down the dorsum to avoid any tension. Ribbon gauze is wound round the penis and soaked in paraffin. This dressing keeps the organ straight, and is left on for about ten days.

##### II. Construction of the new urethra, preferably at about 4 years of age.

(1) A Malecot self-retaining catheter is passed into the bladder.

(2) The catheter is made to protrude in the perineum by reversing the curve of the introducing sound.

(3) It is cut down upon by a diathermy knife, and as soon as a speck of rubber is seen the catheter is forced out through the floor of the urethra, thus leaving a very small hole.

In our hernia work we owe much to the use of penicillin, as serious sepsis in the wound and sinus formation have been eliminated.

This operation is applicable to all types of inguinal hernia—direct, indirect and recurrent—except the small congenital hernie of children and young adults with good muscular and fascial supports where simple herniotomy, followed by repair of the internal ring, is the procedure of choice.

I set no age-limit on my cases for hernia surgery, and only refuse those in which there are definite contra-indications such as pulmonary tuberculosis, &c.

The important steps of the operation are:

- (1) Crease incision, as it heals well and the scar is flexible and almost invisible.
- (2) Stripping the cremaster muscle from the cord and removing an indirect sac after transfixion and ligation of the neck.
- (3) Suturing the cremaster and transversalis fascia (from the point where the cord issues from the internal ring to pubic spine) to Poupart's ligament.
- (4) The insertion of the floss silk darn from the pubic tubercle to the point where the cord issues from the internal ring and then back again to the symphysis. The first row is inserted along Poupart's ligament and the conjoint tendon, whilst the returning layer is introduced with a wider traverse—rectus sheath to Poupart's ligament.
- (5) Approximation of the cut edges of the external oblique aponeurosis *behind* the cord.
- (6) Ensuring that there is no gap or weak spot where the cord issues through the newly constructed combined rings.

Floss silk is preferred to nylon, fascia lata, kangaroo tendon, stainless steel wire, tantalum wire, stout twisted silk, and other materials, because it is a beautifully soft material consisting of the individual fibrils of natural silk, offering a perfectly pliable framework for the subsequent growth of fibroblasts.

[The precise method of introducing the lattice or darn repair was then shown on the film.]

The silk darn becomes incorporated into the tissues and stimulates the formation of a firm, strong but flexible barrier of fibrous tissue, making the area as strong as the tissues into which the lattice extends.

As the repair—firm but not too tight—is sound in practice and in principle, we allow our patients out of bed on the day following the operation and they are discharged from hospital on the eighth day.

They return to light duty in six weeks and to routine work in two months.

In our hands, the sepsis rate is less than 1%, whilst the recurrence rate has never exceeded 3%.

Our highest recurrence rate was in those cases operated on both sides at the same time; now, we allow an interval of ten days between the operations and this factor alone has done much to improve our results.

## An Operation for Hypospadias

By DENIS BROWN, F.R.C.S.

*Surgeon to The Hospital for Sick Children*

THERE are four simple and obvious requirements for an operation for hypospadias:

- (1) It should be applicable to all degrees of the deformity.
- (2) It should be capable of regular completion before the age at which it becomes important to the child to pass urine in the normal masculine manner. That is the age of 5 years, at which schooling in this country is usually begun.
- (3) It should produce a urethra equivalent in diameter and elasticity with the normal.
- (4) It should be within the power of any competent surgeon, and not need either exceptional skill or exceptional fortune for success.

Without going at length into the immense number of procedures advocated for this condition, it will be evident that no single one of them fulfils the first, second, or fourth requirements, and the various methods of forming a urethra by skin grafts do not fulfil the third.

The method here described I believe to fulfil them all. It turns upon the curious fact that the skin of the penis never forms keloid, nor does the subcutaneous tissue thicken and contract following granulation and healing as is the rule elsewhere in the body. Because of this, if a strap of skin is buried along the line where a new urethra is desired it will automatically form itself into a tube without stricture in diameter nor contraction in length.

testosterone pellets into the surgical wound at the time of the radical mastectomy, so we did not carry out the former experiment.

However, it is very important that an evaluation of the exact amount accomplished by post-operative irradiation be determined. If it has no value, it is important that we stop post-operative irradiation because it definitely adds to the post-operative œdema of the arm.

#### HORMONE THERAPY

The work of the British investigators in the œstrogen field has been most fruitful, and under the influence of Haddow will go far toward arriving at vital conclusions.

Haddow and his co-workers in 1944 were the first to describe the use of the synthetic œstrogens diethylstilbœstrol and triphenylchloroethylene, in a number of neoplastic diseases which included bladder, rectum, testes, breast, &c., and in that same year the Section of Radiology of the Royal Society of Medicine presented a discussion of cases of advanced breast cancer receiving the synthetic œstrogens (*Proc. R. Soc. Med.*, 37, 731).

A Joint Scientific Committee on the use of œstrogens in cancer was formed for the co-ordination of this work by the British Empire Cancer Campaign and the Royal Society of Medicine.

For this type of co-operative effort in America, a sub-committee of the Therapeutic Trials Committee, of the American Medical Association, was set up. There are four of us on this Committee with a permanent secretary or co-ordinator. Our supplies of androgens and œstrogens are distributed and given free to about 20 groups of workers who periodically report. The X-ray films, pathological slides, histories, and follow-up reports go eventually to the Army Medical Museum in Washington, where we of the Committee meet and study the material with our X-ray consultants and consultant pathologists.

At Memorial Hospital we have had experience with both the androgens and œstrogens but we have healed a greater number of advanced breast cases with testosterone.

Credit for first suggesting the use of testosterone in breast cancer should go to Dr. A. A. Loeser, a London gynœcologist. Curiously enough both Loeser and P. Ulrich had an article on the subject in the same issue of *Acta Unio Internationalis Contra Cancrum*, in 1939. Loeser, however, followed up his primary suggestion with 6 additional case reports in 1941. Next year, 1942, my associate, Dr. J. H. Farrow, together with our chemist Dr. H. E. Woodard, made a report. They used small doses, 5 to 25 mg. three times weekly. Loeser, in describing their contribution, states: "Unfortunately he used only small quantities and had no results. He even saw an unfavourable effect with the doses he administered on skeletal metastases." Farrow and Woodard were the first, however, to call attention to the hypercalcœmia which occasionally took place under the influence of testosterone therapy.

Fels, in 1944, was the first to demonstrate that improvement in the destroyed areas of bone had taken place in one of his 3 cases. In the same year we had treated 48 private patients, using 25 mg. of testosterone propionate daily, and had been impressed by the occasional response in this group, particularly those cases with bony metastases. One case with brain metastasis had projectile vomiting; one had chest metastasis, and one liver metastasis.

We felt that the possibilities of this hormone would not be known until larger doses of this expensive drug were employed than had been heretofore. We therefore stepped our dosage up to 200 mg. daily in the beginning, and varied the dose from time to time. We made our first report in 1946. We confirmed the Fels' report of his one case of improvement of bone metastasis. Our X-ray films demonstrated bone repair in several cases.

We organized a hormone team at the hospital, formed for the purpose of making further exploration into the effects of the steroids on human cases of advanced breast cancer. The team consists of the following 12 persons: the principal investigator, 2 associate surgeons, 2 research fellows, 1 consultant on steroid chemistry, 1 physiological chemist, 1 radiologist, 1 clinical fellow, a full-time nurse, a full-time social worker, and a secretary.

We have used different œstrogens, but to date our most satisfactory œstrogen is stilbœstrol. We have chiefly used testosterone propionate by injection.

Our conclusion concerning methyl testosterone is that it is not so effective as the propionate.

In order to ascertain the effect of prophylactic doses, we have also employed testosterone propionate in the wound of approximately 500 radical mastectomies. We are not yet ready to report on these cases, except to say that, as a result of inserting four pellets into the latissimus dorsi muscle, a total of 300 mg. in each case, the patients lost their periods,

## PRE-OPERATIVE IRRADIATION

The controversy is still raging in some countries as to the value of pre-operative irradiation. In an effort to evaluate it, for a period of five years (1935 to 1940), we subjected the operable cases of breast cancer to pre-operative irradiation after first establishing that it was breast cancer by aspiration biopsy. During the five years, we employed differing amounts of X-ray therapy, varying from 1,200 r to 3,600 r per portal. The difficulties of performing the operation multiplied with the increased amount of X-ray dosage. Eventually we obtained very poor wound healing, in those who had over 3,000 r per portal. The radical amputation was made at varying times depending on the healing of the skin after the irradiation. In some instances, we operated one month after the X-ray therapy, while in others, we were unable to operate before six months. This delay factor was important. The five-year results of cure, by giving pre-operative irradiation followed by the radical, were mildly disappointing. I had anticipated that the results would be improved. The survival rate of those operable cases having disease confined to the breast, treated by pre-operative irradiation followed by radical surgery, was 74.9%—in contrast to those treated by the immediate radical 82.2%. And similarly those having disease in the breast and axilla, 40.7% versus 43.5% (see Table II). This experiment was therefore costly in human lives but at least in America it largely sounded the death knell of pre-operative irradiation. One of the great errors was that many who had strongly advocated the use of pre-operative irradiation had diagnosed their cases only on clinical grounds, rather than proving the diagnosis by biopsy.

## IMMEDIATE RADICAL MASTECTOMY FOLLOWED BY IRRADIATION

Following the five-year experiment of pre-operative irradiation followed by radical surgery, we next turned to the immediate radical mastectomy, which we have been doing since then.

If the patient has no microscopic involvement of the axilla we rest our case on surgery alone. Because of the fact that axillary involvement implies a fairly desperate situation, we give post-operative irradiation in those cases having such axillary involvement. If they still menstruate, we give X-ray castration.

The improvement in our five-year cures by this method, over the previous five-year method of pre-operative irradiation followed by radical surgery, is encouraging and even striking. It has given us a renewed faith in surgery.

Our increased rate of cure is due to two factors: Improvement in surgery, the care of the patient and X-ray therapy; and in addition the effectiveness of the campaign to educate the public on early signs of cancer.

A comparison of the results of therapy follows:

TABLE II

|                                                | Breast alone involved |       | Breast and axilla involved |       |
|------------------------------------------------|-----------------------|-------|----------------------------|-------|
|                                                | Survival              | Cure  | Survival                   | Cure  |
| Pre-operative irradiation and radical surgery. |                       |       |                            |       |
| Five-year survival and cure .. ..              | 74.9%                 | 70.8% | 40.7%                      | 32.5% |
| Immediate radical followed by irradiation.     |                       |       |                            |       |
| Five-year survival and cure .. ..              | 82.2%                 | 77.6% | 43.5%                      | 36.5% |

Table II demonstrates the price of delay which is necessary if a thorough course of pre-operative irradiation is to be delivered. This is shown in the groups having axillary involvement where the gain by performing the immediate radical (as against pre-operative irradiation) goes from 43.5% to 40.7%; and involvement in the breast alone from 82.2% to 74.9%. The latter group is particularly striking.

Because the end-results in our experience have proven better by the method of immediate radical mastectomy followed by post-operative therapy, we are now pursuing this course.

We do not know if post-operative X-ray therapy adds anything to salvage. It has always been my impression that post-operative X-ray therapy added from 3 to 5%, but as far as we know, no one has carried out the experiment of comparing the results of operable cases where radical surgery alone was employed, with a similar number of cases where the radical was followed by X-ray therapy—in the same hands or clinic. For some time we have wanted to make this comparison, but at the time we wished to start, hormone therapy came into view, and we were more anxious to start on the hormone experiment of introducing

# Section of Experimental Medicine and Therapeutics

President—Professor G. W. PICKERING, M.A., M.B., F.R.C.P.

[February 8, 1949]

## DISCUSSION: EVALUATION OF RENAL CLEARANCES

Professor R. A. McCance and Dr. J. R. Robinson: *Definitions.*

In renal parlance the term "clearance" is usually applied to the expression  $UV/P$  where  $U$  = the concentration of some substance in the urine,  $V$  the volume of the urine passed per minute and  $P$  the concentration of the substance in the plasma. Since  $UV$  is a rate of excretion the expression  $UV/P$  may be described as a rate of excretion per unit of plasma concentration. One of its values as a test of renal function depends upon this for if urea is being excreted at the same rate by two people, one with chronic nephritis and the other with normal kidneys, the fact that the former has a much higher blood urea reduces the size of the expression  $UV/P$  in proportion to the patient's ability to maintain his blood urea within normal limits.  $UV/P$  also has the dimensions of a volume per unit time and it is in fact the smallest volume of blood which could have contained the amount of the substance excreted in one minute. It may be mentioned here that if the substance whose clearance is being measured penetrates the water of the red cells, it makes little difference to the clearance whether the estimations are made on plasma or whole blood. If, however, the substance is confined to the plasma,  $UV/P$  will have a very different magnitude from  $UV/B$ .

### PHYSIOLOGICAL SIGNIFICANCE

If a substance is filtered off freely through the glomerulus so that the concentration in the filtrate is the same as its concentration in the plasma,  $UV/P$  may be written  $UV/F$ , and if further the substance is neither excreted nor reabsorbed by the tubules the expression  $UV/F$  gives the volume of glomerular filtrate formed per unit of time. The desirability of finding a freely filtrable substance which was not later reabsorbed or excreted by the tubules was appreciated by Rehberg and led Homer Smith and others to a series of investigations which culminated in the suggestion that inulin was treated in this way by the healthy kidney. Other substances of very different composition have since been found which have clearances identical with that of inulin and it is highly probable that all of them are excreted by the normal kidney by one and the same mechanism, and that all of them in health give a measure of the glomerular filtration rate.

If this is assumed to be the case, any filtrable substance with a clearance lower than that of inulin is being actively, or passively, reabsorbed by the tubule cells, and urea, uric acid, glucose and the electrolytes are all treated in this way. If, however, a filtrable substance is found to have a clearance greater than that of inulin, this can only mean that it must be passing into the urine both by glomerular filtration and also by tubular excretion. In man and higher apes exogenous creatinine is such a substance, but in lower animals the exogenous creatinine and the inulin clearances are identical and in these animals creatinine is frequently administered to measure the glomerular filtration rate. No other physiological substance has a clearance greater than that of inulin, but certain foreign substances such as diodone, para-amino-hippuric acid, penicillin and phenol red have clearances which are enormously greater than the simultaneous inulin clearances. Of these diodone and para-amino-hippuric acid have plasma clearances of over 600 c.c./min. in normal adult man whereas those of inulin are only of the order of 120 c.c./min. It seems further to have been established by the work of Homer Smith and others that the excretion of diodone is so efficiently carried out by the tubules that when its concentration in the blood is low practically the whole of it is removed from each c.c. of plasma passing through the tubular system of blood-vessels. It follows that its clearance measures the renal plasma flow. The rate of excretion of diodone by the tubules, when the plasma levels are so high that the tubules are fully saturated with the compound—the so-called diodone  $T_m$ —has been used as a measure of the tubules' functional capacity. This quantity has also been referred to as the "tubular excretory mass" (Smith *et al.*, 1938). But it is obvious that it can only be used as a measure of the gravimetric amount of functional tubular tissue if the excretory capacity of such tissue does not vary. Whatever may be the case in the normal kidney, this would seem to be a most dangerous and quite unwarrantable assumption to make when the kidney is disorganized by any pathological process. It was unfortunate that the term "mass" was used to describe this test of function for many have been misled by it into believing that the test gave a measure of the anatomical quantity of functional tubular tissue.

The urea clearance occupies a position of clinical importance because of its frequent use



returned in November 1947, and with diminution in pain, narcotic requirements diminished. Complete function returned after eight months at which time narcotics were discontinued. Repeated X-rays taken as recently as February 1949 reveal no progression of osseous metastases. Patient has had no hormone therapy for twenty months, and she is doing her own housework. Patient has been under observation for four years.

Her dense bony repair of the left ala of the sacrum at the end of four years is interesting (see fig. 1).



FIG. 1.—On admission four years ago there was almost complete absorption of the left ala of the sacrum, with inability to walk or stand without great pain. Under testosterone therapy dense callous was laid down at this site as revealed by the X-ray film taken four years later. The area of repair is more dense than the surrounding normal bone. All clinical symptoms of previous bone destruction are gone.

Our experience with oestrogen has not been as striking as this. Our dosage for stilboestrol is 15 mg. daily for an indefinite period. We have found that oestrogen therapy in many cases requires months before improvement takes place. However, we have seen epithelialization of a cancer ulcer take place within five weeks in one case.

Our dosage at present for testosterone propionate is 100 mg. three times a week given for an indefinite time. We have no suggestion at present as to how to overcome all the unpleasant side-effects. However, there is every probability that a new chemical agent will be developed which will have the same beneficial effect without the mentally distressing side effects.

There are approximately six hundred chemical compounds which should be investigated on human cases of breast cancer. I think we must look chiefly to the steroid chemists and the endocrinologists to be the leaders in this lengthy investigation. We clinicians can be of great help but the endocrinologist is more apt to see the weakest link in the endocrinological chain. During the past five years it has been demonstrated that the life-history of breast cancer has been profoundly altered. I have every belief that great contributions will continue to be made in the next few years.

Indeed, as Beyer (1947) has shown, it may in the case of caronamide be the same as inulin and yet depress both para-amino-hippuric acid and phenol red. As confirmatory evidence, the curves of their excretion show the typical form of a three-component system (Barclay *et al.*, 1947). Thus, in certain important respects, Cushny's two-component theory fails and thereby requires us to make not so much a valuation of renal clearances as a re-evaluation in the light of the rapidly accumulating evidence.

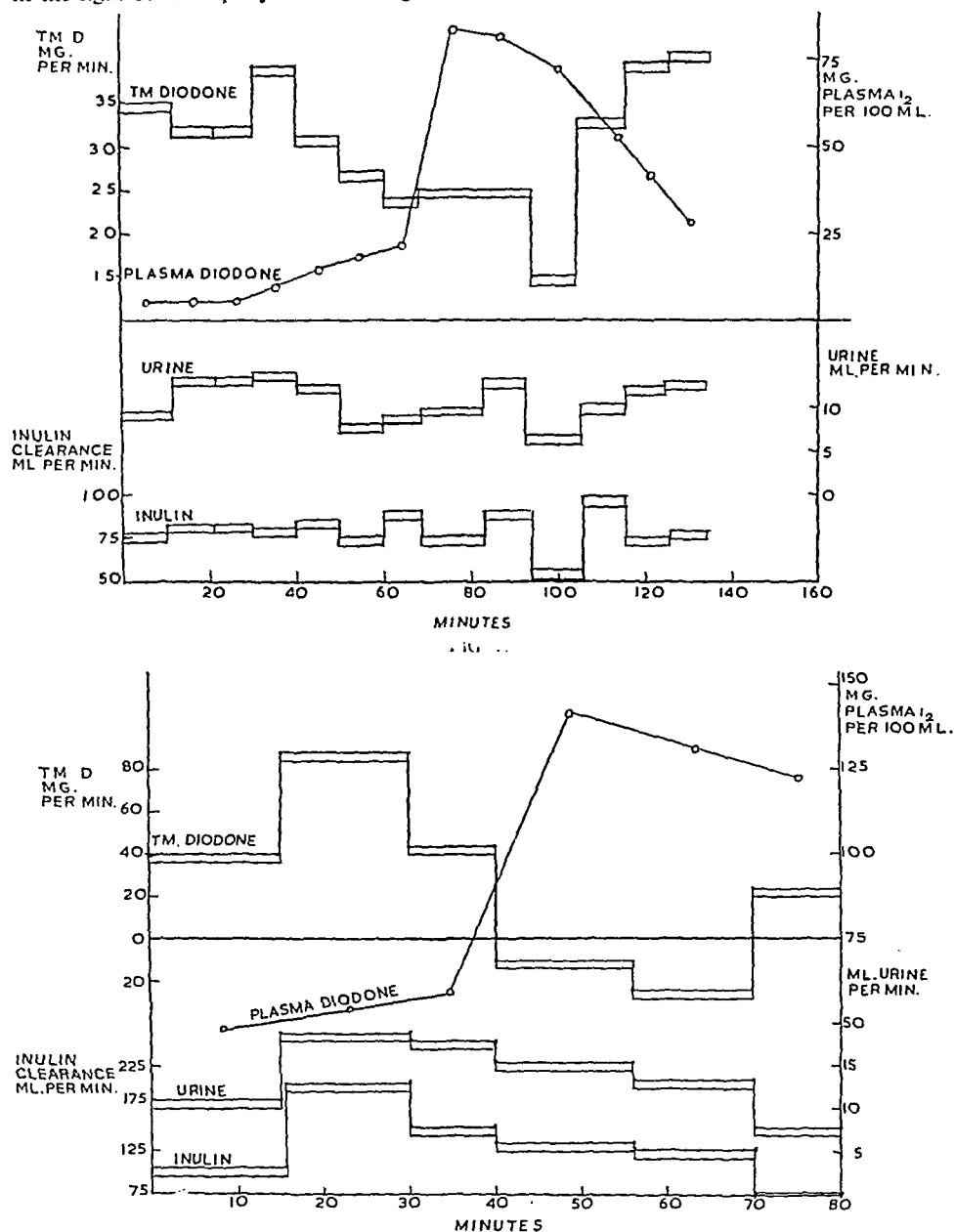


FIG. 2.

FIGS. 1 and 2.—Graphs showing the relationship between the increasing plasma levels Diodone and Tubular Mass. In both cases, Tubular Mass is depressed and, in Fig. 2, falls to negative values.

crept in, for Marshall (1923) in America and Davies *et al.* (1922) in this country suggested that the simple hypothesis would not cover the facts and that only a three-component system, i.e. filtration, reabsorption and secretion, would do so. Cushny, impressed by the experimental evidence offered in support, nevertheless pleaded that "it should be held in reserve, to be invoked only if the simpler view I have presented proves inadequate; and perhaps not even if it fails in obscure and occasional cases but only if it fails all along the line". It would be difficult if not impossible to show that the hypothesis breaks down all along the line, but it is only necessary to show that it breaks down in important instances to compel reconsideration.

Rehberg, in 1926, showed that it was possible to measure filtration rate and consequently reabsorption and, if it occurred, secretion. The importance of Rehberg's work cannot be overestimated. Renal physiology which till then had been qualitative became quantitative. This is not to be taken as dismissing the work of the older workers; most of it, although precise measurements were impossible, was of a high standard. Rehberg studied the reabsorption of urea, chloride and glucose. The reabsorption of urea, he felt, could be explained by simple diffusion but chloride was more difficult since it behaved in different ways at different plasma levels. Glucose reabsorption was determined by its concentration gradient from urine to blood. So that with the substitution of quantitative for qualitative methods, Cushny's hypothesis became less simple. The next important advance was the establishment of secretion by the tubules. Any substance which is secreted should at some blood level be cleared from the blood completely, and at that level measure blood flow. If its level in plasma is raised then on general principles a point should be reached at which the cells are secreting maximally and that amount will be a fixed quantity. We see then that the two-component theory was carried over to this aspect of kidney behaviour. There could be filtration and secretion or filtration and reabsorption but not all three.

In fact, the first substance whose secretion was established with certainty, phenol red, presented a difficulty which has always been neglected, possibly owing to Cushny's advice. Phenol red should measure plasma flow, the value of its  $T_m$  indicates that it should be undoubtedly doing so up to a plasma level of 5 mg. % but, even at the lowest plasma levels, it only measures 80% of the plasma flow. It is true that there are difficulties as to the extent of protein binding and whether bound phenol red is available for excretion, but making full allowances for these, the only explanation of the behaviour of phenol red is that it is filtered, secreted and reabsorbed. When first examined, para-amino-hippuric acid and diodone appeared to behave according to the rules. With continued use, doubt has crept in. It has been shown that in animals following anoxia or poisoning, negative  $T_m$ s or clearances less than inulin could occur (Van Slyke, 1948). In man similar findings have been encountered (Redish *et al.*, 1947). Such behaviour was put down to back diffusion, although just why these substances should leak quicker than inulin is difficult to understand. Our interest in the problem arose when we were attempting to measure  $T_m$ s during exercise in healthy students. The results we attained were not capable of interpretation. Shortly after, we found on a healthy individual, whose renal function has been frequently examined, a negative  $T_m$ . Accordingly, we pursued the matter further on a series of healthy subjects and on a number of patients. Both diodone and para-amino-hippuric acid were used. It was found that as plasma level is raised, there is a gradual increase in  $T_m$  until at some plasma level there is a collapse of  $T_m$  to low or negative values, with recovery if plasma level once more falls (figs. 1 and 2). Again, the most likely explanation of these facts is that, under certain circumstances, these substances are also excreted by a three-component system.

There are two other ways of examining this matter. If what we term the index (Barclay and Kenney, 1946) is used (in most cases plotting the ratio of the clearance of the substance against inulin will give the same information) it can be shown that combining the curves describing the behaviour of a reabsorbed substance and the curve for a secreted substance, a third curve is obtained which describes the behaviour of a three-component substance. A curve of this particular shape cannot be due to any other system of excretion, and the actual level of the curve, that is whether it exceeds inulin or not, does not affect the interpretation. If phosphate is examined at rising plasma levels, its excretion both in man and dog is described by such a curve (Barclay *et al.*, 1947). It is of interest that it was the work of Davies *et al.* and Marshall on phosphate that forced Cushny to reconsider his hypothesis. If one examines the figures of McCance (1937) for potassium it is evident that here, too, we are dealing with a three-component system and since we first drew attention to this, two papers have appeared confirming this and thereby vindicating the value of the curve (Mudge *et al.*, 1948; Berliner and Kennedy, 1948). Urea, when plotted, also gives evidence that further examination will show that it too is three component.

The other way of examining the matter is to find what effect a substance known to be secreted has on the substance being examined. It is well established that there is mutual interference between secreted substances. Sulphonamides have been examined by Landquist (1945) and shown to be depressed by hippuran, and this depression occurs no matter what the initial clearance of the sulphonamide may be, i.e. whether it is higher or lower than inulin.

## Section of Orthopædics

President—H. J. SEDDON, M.A., D.M., F.R.C.S.

[December 7, 1948]

### The Treatment of Prostatic Secondary Deposits in Bone

By E. W. RICHES, M.C., M.S.

*Middlesex Hospital*

*Occurrence.*—The prostate is one of the sites of primary carcinoma from which metastases in bones may be expected; Muir (1934) found them present in 28% of autopsy cases. One year ago (Riches, 1948) I mentioned 40 clinical cases of carcinoma of the prostate treated for three years and upwards where osseous metastases were present in 15, a percentage of 37·5. I propose to base my remarks mainly on the survivors of the same 15 cases; 6 were alive a year ago and 5 are still alive. They have now all been under treatment for at least four years, and two of them for over five years. Subsequent patients treated more recently have followed a similar clinical course.

*Site.*—The bones of the pelvis are those most frequently invaded, but the vertebræ, ribs, femora, clavicles and skull may be involved later. Batson (1940) has demonstrated a plexus of veins investing the sacrum, ilia and lumbar spine and having connexions with the prostatic plexus. He suggested that spread by this vertebral system of veins is the only satisfactory explanation of the often symmetrical deposition of secondary deposits in these bones from carcinoma of the prostate. In the 15 cases under review the pelvis or lumbar spine was certainly involved in 14; the remaining patient developed secondaries in the lungs and ribs whilst away in the country and his pelvis was not X-rayed. From the diagnostic point of view one can be content with films showing the pelvis and lumbar spine; if these are not invaded there is no point in having the numerous X-rays of the whole skeleton which we see so often.

*Type.*—Osteoplastic or sclerosing secondaries are commoner than the osteolytic or destructive type; I have no evidence that the latter respond to treatment better than the former.

## REFERENCES

- BARCLAY, J. A., and KENNEY, R. A. (1946) *Acta med. Scand.*, **125**, 385.  
 —, COOKE, W. T., and KENNEY, R. A. (1947) *Acta med. Scand.*, **128**, 500.  
 BERLINER, R. W., and KENNEDY, T. J. (1948) *Proc. Soc. exp. Biol.*, **67**, 542.  
 BEYER, K. H., RUSSO, H. F., PATCH, E. A., TILLSON, E. K., and SHONER, G. (1947) *J. Pharmacol.*, **91**, 272.  
 CUSHNY, A. R. (1917, 1926) *The Secretion of the Urine*. London.  
 DAVIES, H. W., HALDANE, J. B. S., and PESKETT, G. L. (1922) *J. Physiol.*, **56**, 269.  
 LANDQUIST, F. (1945) *Acta Pharm. Toxic.*, **1**, 307.  
 McCANCE, R. A., and WIDDOWSON, E. M. (1937) *Lancet* (ii), 247.  
 MARSHALL, E. K., and CRANE, M. M. (1923) *Amer. J. Physiol.*, **64**, 387.  
 MUDGE, G. H., FOULKS, J. G., and GILMAN, A. (1948) *Proc. Soc. exp. Biol.*, **67**, 545.  
 REDISH, J., WEST, J. R., WHITEHEAD, B. W., and CHASIS, H. (1947) *J. clin. Invest.*, **26**, 1043.  
 REHBERG, P. B. (1926) *Biochem. J.*, **20**, 447 and 461.  
 VAN SLIKE, D. (1948) *Ann. intern. Med.*, **28**, 701.

**Dr. D. A. K. Black:** If the renal circulation can be altered in the radical way described by Trueta and his co-workers, it is obviously important to consider the changes which the occurrence of a shunt in the kidney would occasion in renal clearances. With Drs. M. G. Saunders and S. Oleesky, I have observed some of the effects of possible shunt-producing stimuli on renal clearances, and on the directly observed renal venous outflow in cats and rabbits. In one series, the abdomen was not opened, but clearance of inulin and para-amino-hippurate (PAH) was measured before, during, and after sciatic stimulation. About half the animals showed no change in clearance; the others showed a definite fall in both inulin and PAH clearance, the ratio  $C_{in}/C_{PAH}$  being commonly increased. Since observations of this type cannot give clear proof of a shunt in the kidneys, a further series of experiments was devoted to observing the renal venous flow by direct methods; at the same time, the extraction of PAH by the kidney was measured. It was found that in some cases PAH extraction might be greatly reduced, although the renal blood flow was within normal limits. This could scarcely be due to "tubular anoxia", and the most likely explanation seems to be that a great part of the renal blood was failing to perfuse secretory parts of the tubules. In such circumstances, the equation of PAH clearance with renal blood flow loses all meaning.

**Dr. W. T. Cooke:** Dr. Barclay and I have studied a number of patients in whom urea clearance has been greater than inulin clearances which varied 20-50 ml. per minute, and in some of these cases the urea clearance has been greater than the simultaneous inulin endogenous creatinine and diodone clearances. It seems unlikely that such a finding can be explained by the back diffusion of three different and larger molecules at a rate faster than the relatively simple and freely diffusible molecule of urea. It is probable, therefore, that urea in such cases is actually secreted by the tubules, an observation which would be in keeping with much of Oliver's work on the nephron in chronic kidney disorders. In passing, one might add that the use of the term "diffusion" as applied to the processes of reabsorption in the tubules needs reconsideration since relative rates of reabsorption bear no relationship whatsoever to various diffusion constants of the solutes.

**Professor Robert Platt:** In answer to Professor McCance's question as to the value of modern clearance studies in clinical work, I would say that they do not tell us anything with regard to diagnosis and prognosis which cannot be as well assessed by simpler tests such as urea clearance, but they were never intended to do so. One had hoped that by clearance studies in renal disease we should have gained rather more knowledge of the functional pathology of the kidney in various disorders. Although, in general, there appears to be a low filtration fraction in acute nephritis, and a high one in hypertension and in chronic renal failure, the interpretation of diodrast and PAH clearances in renal disease is subject to many errors. In the very few papers which deal with clearance tests in chronic renal disease the brief clinical data recorded lead one to doubt whether the results are of any value at all. An attempt has usually been made in such papers to find a pattern of renal function characteristic of chronic nephritis without distinguishing between the oedematous phase of Type II nephritis and the terminal (azotæmic) phase of other forms of renal failure.

**Professor H. P. Himsworth:** Have we not been in danger of assuming that renal clearances are specific tests of kidney function? A normal renal clearance depends upon possessing, not only a normal kidney, but a normal circulation, a normal electrolyte and water metabolism and probably many other factors. Thus it is a commonplace that in heart failure the clearances may be grossly abnormal while tests of the concentrating power of the kidney show clearly that there is no impairment of renal function. Renal clearance tests are in fact not tests of kidney function but tests of the total capacity of the body to excrete into the urine; and in that capacity renal function is only one component. Clearances can, therefore, be interpreted as renal function tests only on the assumption that other relevant systems are normal. The validity of making that assumption in many clinical conditions is open to question.

the second lumbar vertebral body by osteolytic secondaries (fig. 2). He was admitted as a dying man but a resumption of stilbæstrol followed by X-ray therapy produced a gradual but definite clinical improvement. Consolidation has taken place and after more than a year the condition has stabilized (fig. 3). He is still alive and able to



FIG. 2.—Osteolytic secondaries in L.2.



FIG. 3.—Same case as fig. 2 thirteen months later.

walk three years after his first treatment and two and a half years after the vertebral collapse.

When bony metastases are present it is advisable to continue a high maintenance dose for a longer period; unpleasant side-effects such as painful swelling of the breasts are usually relieved by a slight reduction of the dose, and if nausea is produced dienæstrol may be substituted for stilbæstrol, although it is not always so effective.

X-ray treatment has sometimes proved a useful adjuvant to stilbæstrol; it is my practice in most cases to reserve it for patients whose pain persists and it has often had a marked palliative effect. Some cases have been treated from the beginning with X-rays to the primary growth as well as stilbæstrol but their clinical course has

**Detection.**—The first indication of the presence of deposits in bone is given by the symptom of pain, sciatic or lumbar in distribution, and often worse on sitting down. Confirmation is obtained by the X-rays of the pelvis and lumbar spine which are taken in all cases of suspected carcinoma of the prostate. Before treatment is started the serum acid phosphatase should be estimated; a raised value (above 3 units) is found in most untreated cases with bony deposits, and considerable elevation (above 10 units) is almost pathognomonic, although the value may also be high when there are lymphatic or visceral metastases. It was raised in 9 out of these 15 cases, but some had received previous treatment. The main use of the test is in checking the response to treatment whether by oestrogens or X-ray therapy. Fig. 1 shows the levels in a case

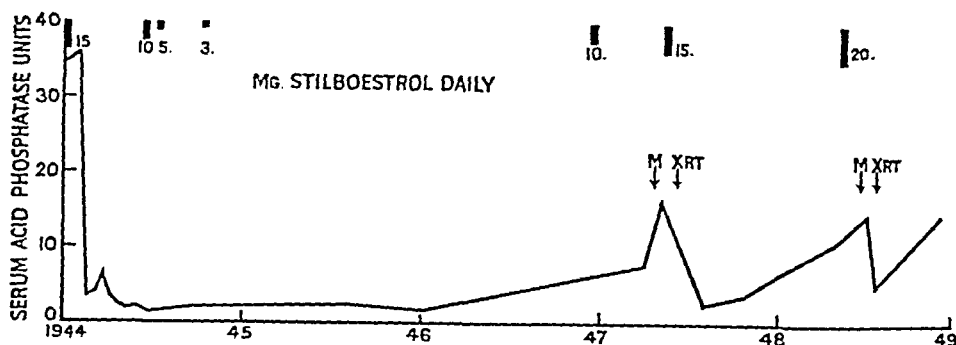


FIG. 1.—Five-year record of acid phosphatase in a patient with secondary deposits in bone from carcinoma of the prostate. M = New metastases discovered. XRT = X-ray therapy.

followed for five years; elevation of the serum acid phosphatase is taken as an indication for more intensive treatment. This is an extension over a longer period of the previous graph (*Proc. R. Soc. Med.*, 41, 49).

**Course.**—Before the use of oestrogens the occurrence of osseous metastases was rightly regarded as an indication of impending death. Pain could sometimes be relieved by X-ray therapy but the patient was often bedridden and the general course was downhill.

**Treatment.**—The methods of treating bony metastases are by oestrogens (or castration) and by X-ray therapy. The first essential in treating every case of carcinoma of the prostate is to relieve any gross urinary obstruction which may be present. This can be done slowly by means of oestrogens, or more quickly and effectively by endoscopic resection of the prostate. I prefer the latter method as it gives tissue for histological confirmation of the disease as well as providing an adequate urinary channel. Oestrogens seem to be more effective than castration and may be started before operation provided blood has been taken for a serum acid phosphatase determination. My usual practice is to start with 1 mg. of stilboestrol t.d.s. with daily increments of 1 mg. per dose up to 5 mg. t.d.s. This is maintained until the clinical condition and fall in acid phosphatase suggest that it may safely be reduced, but it cannot be stressed too strongly that a maintenance dose is necessary for the rest of the patient's life. Too often the dramatic improvement so frequently seen is taken by the patient or his doctor as an indication to stop treatment.

A man of 51 was treated by endoscopic resection and stilboestrol for carcinoma of the prostate in June 1946; X-rays showed no bony metastases and he left hospital taking 15 mg. of stilboestrol daily. After four months he was told by his doctor he could stop taking the tablets; he came back after nine months with destruction of

however, it is possible to detect changes; they can be seen in the original films better than in reproductions or slides. Osteoplastic areas become reduced in density and the bone structure tends to return to normal. Fig. 4 shows a localized sclerosis in the right ischium in a man bedridden with sciatica; he developed multiple secondaries in the lungs which subsequently disappeared but after two and a half years (fig. 5) the area of density in the ischium was reduced and he remains well over four years since treatment started on 9 mg. of stilbæstrol daily, having taken over 16,000 mg. in all.

The highest value of acid phosphatase was 85 units and was recorded in one case with extensive osteoplastic deposits in the pelvis and spine; secondaries were found subsequently in the femora (fig. 6) and in the ribs. After three and a half years there was diminution in density of the deposits in the pelvis and he remains well five years after the onset, still taking 15 mg. of stilbæstrol daily and having taken more than 24,000 mg. altogether. The acid phosphatase came down to normal limits after 3,000 mg.

In the case of osteolytic secondaries improvement is shown radiologically by an increase in density of the bone. My longest case with bone metastases is alive five years one month since starting treatment. He was found to have pelvic metastases, mainly osteolytic in type, and most marked near the left acetabulum (fig. 7). I have



FIG. 7 (25.1.44).—Osteolytic deposits.  
(Figs. 7 to 11 illustrate the case recorded in fig. 1.)

a fairly complete record of the changes in his pelvis throughout the period; there was a gradual increase of sclerosis in the affected areas during the first year (fig. 8). In the thirteenth month he had the misfortune to fracture the neck of the right femur which was not affected by secondaries. This was pinned by Mr. O'Connell and united firmly (fig. 9); he remained well for more than three years when he began to lose weight and get pain in his right hip; the acid phosphatase was rising (fig. 1) and new metastases were found in the right side of the pelvis (fig. 10); increase of dosage back to 10 mg. daily failed to relieve his pain but with 15 mg. daily and a course of X-ray treatment he improved greatly; the acid phosphatase fell to normal again. He regained some weight and the affected areas in the pelvis showed more



not been materially altered. I have never seen a fall in acid phosphatase from X-ray treatment alone, and this is one of the main indications of response to therapy.

*Prevention of metastases.*—Whilst œstrogens have an undoubted effect in controlling metastases they are not always successful in preventing them; in 4 cases of this series secondaries in bone appeared during the course of treatment. In one case there was a large, hard gland in the neck which disappeared after four and a half months; after nine months there were osseous deposits in the pelvis, but he lived for three and a



FIG. 4.—Osteoplastic secondary in right ischium.



FIG. 5.—The same case as fig. 4 two and a half years later.

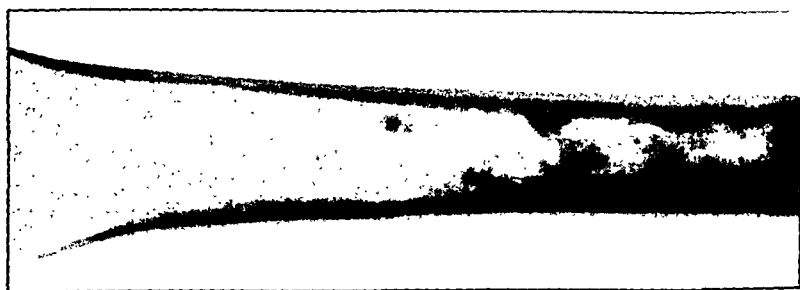


FIG. 6.—Scattered deposits in the femur.

half years. One case developed deposits in the right ilium and pubis after seven months, but lived for four years; another developed a sclerotic metastasis in the fourth lumbar vertebra after nine months; it responded well to an increased dose of œstrogen and was no longer detectable after two and a half years. He remains well and working four years and seven months after starting treatment. The fourth case stopped taking stilbœstrol after a year, and after three and a half years had secondaries in the lungs and ribs. When stilbœstrol was resumed these disappeared and he is alive more than five years after starting treatment. The disappearance of pulmonary metastases is more readily demonstrated by X-rays than that of osseous deposits; in the bones,

There comes a time for all cases when stilbœstrol ceases to have an effect and an increase of dose produces no further benefit. In one such case where the skeleton was riddled with metastases we gave 50 mg. daily with the addition of 40 mg. of soluble dienœstrol intravenously without effect, but this was after more than two

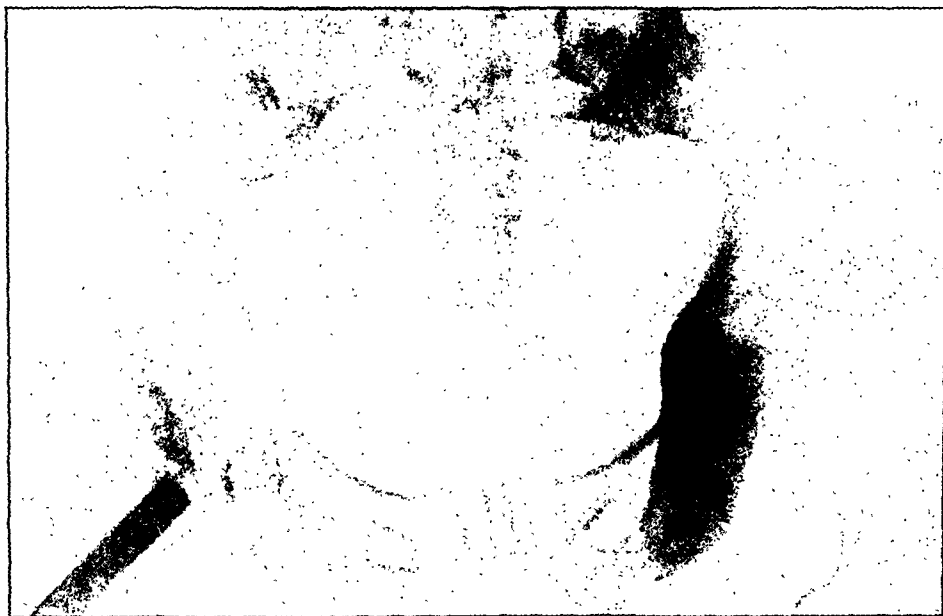


FIG. 10 (11.4.47).—New osteolytic deposits in right side of pelvis.



FIG. 11 (2.6.48).—Some new areas of destruction are appearing on the left side.

years of treatment. In general there is a tendency to give too small a maintenance dose, and I do not agree that a higher dose produces earlier resistance to œstrogens.

consolidation. After four and a quarter years the acid phosphatase was rising again despite a maintenance dose of 15 mg. of stilbæstrol daily and there was still rarefaction about the right acetabulum. The dose was increased to 20 mg. daily and he was given more X-ray treatment which again relieved his pain. The phosphatase fell but the pelvis showed little further change (fig. 11), and there was evidence of deposits in



FIG. 8 (24.11.44).—Regression of secondaries with consolidation.

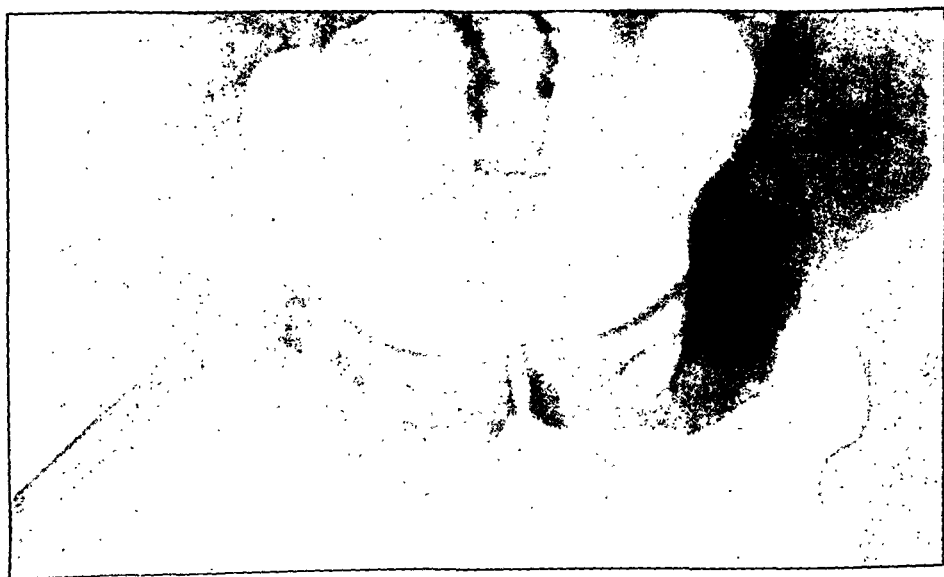


FIG. 9 (5.7.46).—Further sclerosis on the left. Fracture of neck of right femur.

the lungs and ribs. Nevertheless, on a continued maintenance dose of 20 mg. daily, he kept going until he sustained a spontaneous fracture of the shaft of the left femur five and a quarter years after treatment started. The acid phosphatase was 14.8.

POSTSCRIPT.—This patient died 16.6.49, 5 years and 8 months after treatment started.

There comes a time for all cases when stilbæstrol ceases to have an effect and an increase of dose produces no further benefit. In one such case where the skeleton was riddled with metastases we gave 50 mg. daily with the addition of 40 mg. of soluble dienæstrol intravenously without effect, but this was after more than two



FIG. 10 (11.4.47).—New osteolytic deposits in right side of pelvis.



FIG. 11 (2.6.48).—Some new areas of destruction are appearing on the left side.

years of treatment. In general there is a tendency to give too small a maintenance dose, and I do not agree that a higher dose produces earlier resistance to æstrogens.

consolidation. After four and a quarter years the acid phosphatase was rising again despite a maintenance dose of 15 mg. of stilbæstrol daily and there was still rarefaction about the right acetabulum. The dose was increased to 20 mg. daily and he was given more X-ray treatment which again relieved his pain. The phosphatase fell but the pelvis showed little further change (fig. 11), and there was evidence of deposits in

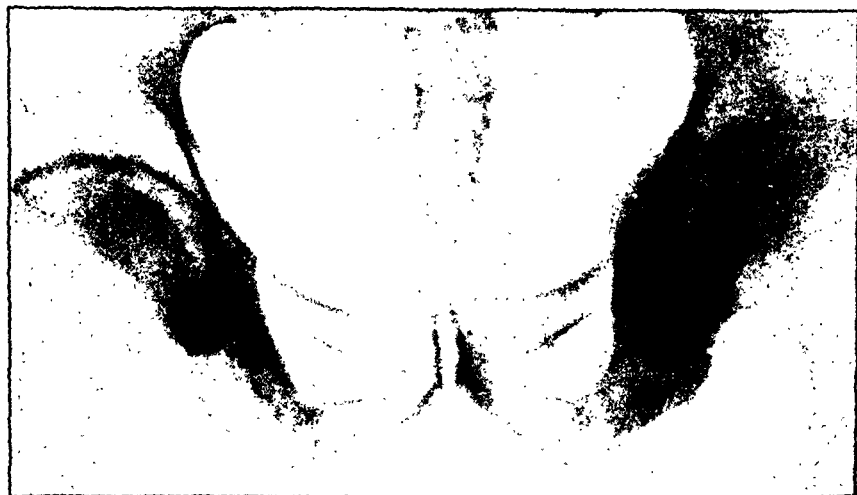


FIG. 8 (24.11.44).—Regression of secondaries with consolidation.

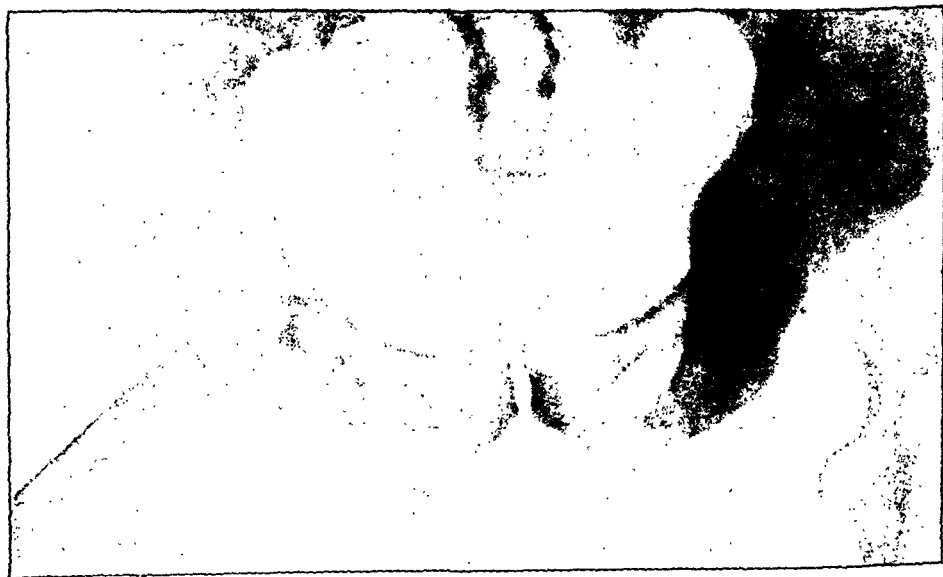


FIG. 9 (5.7.46).—Further sclerosis on the left. Fracture of neck of right femur.

the lungs and ribs. Nevertheless, on a continued maintenance dose of 20 mg. daily, he kept going until he sustained a spontaneous fracture of the shaft of the left femur five and a quarter years after treatment started. The acid phosphatase was 14·8.

POSTSCRIPT.—This patient died 16.6.49, 5 years and 8 months after treatment started.

There comes a time for all cases when stilbæstrol ceases to have an effect and an increase of dose produces no further benefit. In one such case where the skeleton was riddled with metastases we gave 50 mg. daily with the addition of 40 mg. of soluble dienæstrol intravenously without effect, but this was after more than two



FIG. 10 (11.4.47).—New osteolytic deposits in right side of pelvis.



FIG. 11 (2.6.48).—Some new areas of destruction are appearing on the left side.

years of treatment. In general there is a tendency to give too small a maintenance dose, and I do not agree that a higher dose produces earlier resistance to æstrogens.

We must remember that X-rays do not give the whole clinical picture; even the patients who have only survived for two years have often spent them as useful citizens instead of bedridden chronic invalids, and this disease affects those who are already elderly.

As an orthopædic problem one may meet it as a rare cause of spontaneous fracture, but its main interest for orthopædist must be in diagnosis; it provides an illustration of the fact that all cases of sciatic pain are not due to disc lesions.

#### REFERENCES

- BATSON, O. V. (1940) *Ann. Surg.*, **112**, 138.  
MUIR, E. G. (1934) *Lancet* (i), 667.  
RICHES, E. W. (1948) *Proc. R. Soc. Med.*, **41**, 47.

### Electrical Reactions of Muscle in Poliomyelitis

BY IAN G. MACKENZIE, M.D.

In any condition in which muscle paralysis or weakness is a feature, the electrical reactions of the affected muscles give an indication of the integrity of the nerve cells and axons supplying them. In poliomyelitis, we know that reversible changes occur in some anterior horn cells while others are completely destroyed (Bodian, 1947). If it were possible to distinguish these two types of paralysed muscle at an early stage of the disease, not only would the patient benefit from an early prognosis, but the treatment might well be modified. From a study of 35 cases over the past twelve months, it appears that such a distinction is possible, and this incomplete survey is given in the hope that it will encourage others to carry out this examination on cases of poliomyelitis in which prolonged observation is possible.

The determination of the Strength-Duration curve is generally recognized as the best method of studying the excitability of voluntary muscle. In order to excite muscle, an electrical stimulus must be of sufficient strength and duration, and its rate of change from zero to an effective height must be sufficiently rapid. Stimulators have been devised (Bauwens, 1941; Conrad, Haggard, and Teare, 1936; Ritchie, 1944; Walter and Ritchie, 1945) which deliver impulses of varying strengths at several durations, impulses whose voltage rises virtually instantaneously from zero; using such a stimulator, one can ignore the rate of increase of the stimulus, and express excitability purely in terms of strength and duration of a minimal stimulus as a curve showing the threshold strengths of stimuli of varying duration. Such a curve is the Strength-Duration curve.

The various types of stimulators available and the technique of examination (Ritchie, 1944a) need not concern us at the moment. Fig. 1 shows the curve obtained from normal muscle. It is smooth in shape, rising steeply at the shorter durations of stimulus. Various points on this curve may be used as a basis for comparison with other curves. The *rheobase* is the threshold voltage of a stimulus of infinite duration; this is low. The *threshold voltage at 0.5 millisecc.* is a convenient index of the threshold at shorter duration of stimulus; it is but little higher than the rheobase in normal muscle, which is simply another way of saying that the curve is flat at long durations of a stimulus. The third index, the *chronaxie*, is the threshold duration of a stimulus of twice rheobasic strength; it is short for normal muscle.

Variations of this curve occur under abnormal conditions. Fig. 2 shows the curve of denervated muscle. There is a (sluggish) response to long duration stimuli only.

The rheobase and chronaxie are both high. A somewhat similar curve is obtained from muscle on the point of recovery, but the characteristic of the curve of denervated muscle is that it is permanent.

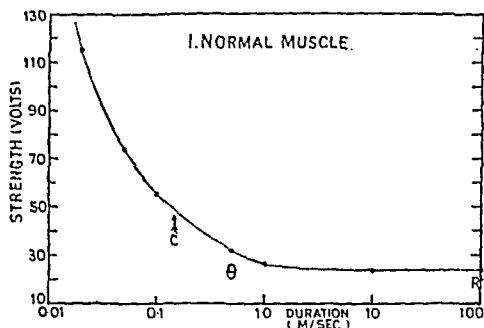


FIG. 1.—R = Rheobase. C = Chronaxie.  
 $\Theta$  = Threshold voltage at 0.5 m/s.

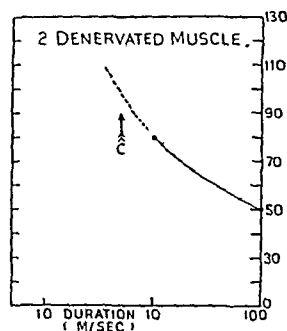


FIG. 2.—A similar short, steep, high curve is seen in a muscle about to show early clinical signs of recovery.

In peripheral nerve injuries, this curve is apparent in three weeks, but in poliomyelitis its rate of appearance varies considerably. The longest time that we have seen is twelve weeks after the onset of the disease. A possible explanation of this delay might be that some cells damaged by the disease only finally die as a result of some added insult such as excessive early exercise—and some evidence in support of this is given by a study of these curves.

When a muscle is denervated, the Strength-Duration curve does not gradually alter from the normal form to that of denervated muscle (Bauwens, 1943; Marble, Hamlin, and Watkins, 1942; Pollock, Golseth, and Arieff, 1944, 1945, 1945a; Pollock, Golseth, Arieff, Sherman, Schiller, and Tigley, 1945b). During the process of degeneration, the curves tend to move from those of normal muscle to those of denervated muscle, but the position of the curve varies from day to day until a final stable state is reached. It is this fluctuation of the curves, even though it occurs in a regular manner, which makes the interpretation of results difficult if an isolated examination only is made at an intermediate stage of the disease.

There is, however, one fundamental difference which enables a distinction to be made between the curves of a muscle that will recover and those of a muscle that will not. *In a muscle that is going to recover the curves remain essentially normal in shape, in the early stages of the disease*, even though their position may alter; that is to say even though higher voltages than normal are required to elicit a response. *In a muscle that will not recover, the shape of the curve is abnormal*, although the threshold voltages at long durations of stimulus may be even lower than normal.

*The optimum time for making this distinction, that on which the prognosis is based, is probably the fourth week after the onset of the disease.* By then the changes in the anterior horn cells are said to be maximal (Bodian, 1947), and it is then still relatively easy to differentiate the two types of curve.

Fig. 3 shows the two types of curve at the fourth week after the onset of the disease. A good prognosis is given on a curve which is normal in shape, but where the threshold voltages are higher than normal; that is to say a curve with a high rheobase, little difference between the rheobase and the threshold at 0.5 millise., and a short chronaxie. A bad prognosis is given on a curve which is abnormal in shape, even though the threshold voltages at long durations of stimulus may be quite



We must remember that X-rays do not give the whole clinical picture; even the patients who have only survived for two years have often spent them as useful citizens instead of bedridden chronic invalids, and this disease affects those who are already elderly.

As an orthopædic problem one may meet it as a rare cause of spontaneous fracture, but its main interest for orthopædist's must be in diagnosis; it provides an illustration of the fact that all cases of sciatic pain are not due to disc lesions.

#### REFERENCES

- BATSON, O. V. (1940) *Ann. Surg.*, **112**, 138.  
MUIR, E. G. (1934) *Lancet* (i), 667.  
RICHES, E. W. (1948) *Proc. R. Soc. Med.*, **41**, 47.

## Electrical Reactions of Muscle in Poliomyelitis

BY IAN G. MACKENZIE, M.D.

In any condition in which muscle paralysis or weakness is a feature, the electrical reactions of the affected muscles give an indication of the integrity of the nerve cells and axons supplying them. In poliomyelitis, we know that reversible changes occur in some anterior horn cells while others are completely destroyed (Bodian, 1947). If it were possible to distinguish these two types of paralysed muscle at an early stage of the disease, not only would the patient benefit from an early prognosis, but the treatment might well be modified. From a study of 35 cases over the past twelve months, it appears that such a distinction is possible, and this incomplete survey is given in the hope that it will encourage others to carry out this examination on cases of poliomyelitis in which prolonged observation is possible.

The determination of the Strength-Duration curve is generally recognized as the best method of studying the excitability of voluntary muscle. In order to excite muscle, an electrical stimulus must be of sufficient strength and duration, and its rate of change from zero to an effective height must be sufficiently rapid. Stimulators have been devised (Bauwens, 1941; Conrad, Haggard, and Teare, 1936; Ritchie, 1944; Walter and Ritchie, 1945) which deliver impulses of varying strengths at several durations, impulses whose voltage rises virtually instantaneously from zero; using such a stimulator, one can ignore the rate of increase of the stimulus, and express excitability purely in terms of strength and duration of a minimal stimulus as a curve showing the threshold strengths of stimuli of varying duration. Such a curve is the Strength-Duration curve.

The various types of stimulators available and the technique of examination (Ritchie, 1944a) need not concern us at the moment. Fig. 1 shows the curve obtained from normal muscle. It is smooth in shape, rising steeply at the shorter durations of stimulus. Various points on this curve may be used as a basis for comparison with other curves. The *rheobase* is the threshold voltage of a stimulus of infinite duration; this is low. The *threshold voltage at 0.5 milliser.* is a convenient index of the threshold at shorter duration of stimulus; it is but little higher than the rheobase in normal muscle, which is simply another way of saying that the curve is flat at long durations of a stimulus. The third index, the *chronaxie*, is the threshold duration of a stimulus of twice rheobasic strength; it is short for normal muscle.

Variations of this curve occur under abnormal conditions. Fig. 2 shows the curve of denervated muscle. There is a (sluggish) response to long duration stimuli only.

## Section of Psychiatry

President—J. R. REES, C.B.E., M.A., M.D., F.R.C.P., D.P.H.

[March 8, 1949]

### Pharmacological Explorations of the Personality: Narco-Analysis and Methedrine Shock

By Professor JEAN DELAY, M.D.

(Professor of Psychiatry, Faculty of Medicine, Paris)

#### ABSTRACT

(Full paper in French follows)

THE use of drugs to recall forgotten memories and to explore latent personality tendencies has a long history. "In vino veritas" is an ancient truism. The use of drugs in the study of psycho-pathology is, however, more recent, dating from 1845 when Moreau de Tours published his paper: "Du Hachisch et de l'Aliénation mentale." Moreau reached the important conclusion that the dreams experienced under the influence of hashish were not only comparable but also identical with the hallucinations of psychotic patients. Kant's statement, "A madman is a sleeper awake" was thus paraphrased: "Madness is the dream of a man awake." Further explorations of the personality structure using hashish could well be repeated to-day. Other drugs then came into vogue; but present-day interest is mainly centred on two groups—the sodium barbiturates and the amphetamines (benzedrine and methedrine). That these two groups are antagonistic in their action will be shown in this paper.

The sodium barbiturates have been increasingly used for narco-analysis, particularly during the war, not only in the therapy of acute combat neuroses but also for the diagnosis of malingering. Despite considerable variations in the techniques of their use there is a common basic approach: the exploration of the unconscious. Hughlings Jackson's concept of the release of lower centres from control by higher centres is considered to apply since there is a release of unconscious material, as in dreams. Amongst the techniques a distinction must be made between those in which the doctor is passive, allowing the drug to elicit the unconscious material alone, and those in which he plays an active role, questioning, suggesting and interpreting to the patient. More attention should be given to the psychosomatic aspects of narco-analysis.

The psychotonic action of *d*-phenylisopropylmethylamine or methedrine was first discovered by Hauschild in 1938. Intravenous injection of 30 mg. produces a state best described as "methedrine shock" with severe concomitants, both physical (raised blood-pressure) and psychological. It is twice as powerful as benzedrine.

A comparison between these two groups reveals their antagonistic action. The sodium barbiturates may be classed as "psycholeptic" since they produce a lowering of intra-psychoic tensions and are depressants of psychological tonus. On the other hand methedrine is a "psychagogue", increasing intra-psychoic tension and acting as a stimulant.

#### CASE STUDIES

(1) *Manic-depressive psychosis*.—Manic and depressive states can be relieved for short periods by sodium amytal. Methedrine leads to violent outbursts of excitement and euphoria in the former and of agitation and depression in the latter, and hence is of value in the differential diagnosis of atypical cases. Both drugs are particularly

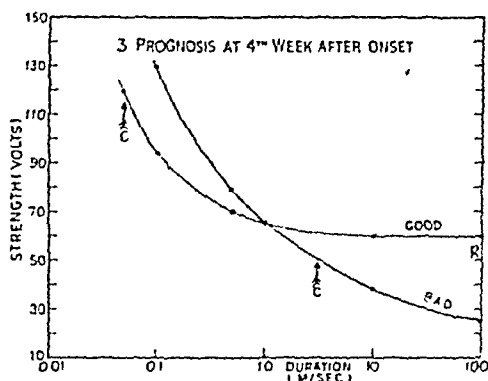


FIG. 3.—The shape of the curve obtained from the muscle as a whole at the 4th week gives an indication of the proportion of viable and non-viable motor units in it, and then of the grade of clinical recovery likely to occur. A good prognosis should not modify treatment, but may make it less arduous. A bad prognosis should be faced *early* by the surgeon who should start rehabilitation of his patients before months of futile treatment have sapped their spirit.

low; that is to say on a curve where the rheobase is low, there is a marked difference between the rheobase and the threshold at 0.5 millise., and the chronaxie is long.

The practical application of these results is obvious. If the prognosis is good, one can contentedly spend long periods of treatment on rest and re-education. If the prognosis is bad, one should proceed at an early date to order any necessary supporting apparatus for the patients, and get them up, thereby saving weary months during which they do little but learn the names of muscles that they will never use.

This is a mere sketch of the subject of electrical reactions in poliomyelitis, and it is given in this incomplete form only because it is believed that some of these patients can be saved unnecessary months of immobilization, and in the hope that others will interest themselves in the problem and prove or disprove the thesis.

#### REFERENCES

- BAUWENS, P. (1941) *Brit. J. Phys. Med.*, **4**, 150.  
 — (1943) *Proc. Roy. Soc. Med.*, **37**, 25.  
 BODIAN, D. (1947) *J. Amer. med. Ass.*, **134**, 1148.  
 CONRAD, A. G., *et al.* (1936) Publication from the School of Engineering, Yale. No. 15.  
 MARBLE, H. S., *et al.* (1942) *Ann. J. Surg.*, **55**, 274.  
 POLLOCK, L. J., *et al.* (1944) *Surg. Gynec. Obstet.*, **79**, 133.  
 — (1945) *Northwestern Medical School Bull.*, **19**, 3, 169.  
 — (1945a) *Surg. Gynec. Obstet.*, **81**, 451.  
 — (1945b) *War Medicine*, **7**, 275.  
 RITCHIE, A. E. (1944) *J. Sci. Inst.*, **214**, 64.  
 — (1944a) *Brain*, **67**, 314.  
 WALTER, W. E., and RITCHIE, A. E. (1945) *Electronic Engineering*, **17**, 585.

Mr. Anthony Green read a paper entitled The General Treatment of Secondary Deposits in Bone.

Mr. A. S. Blundell Bankart showed a film illustrating the Operative Treatment of Recurrent Dislocation of the Shoulder.

Mr. L. S. Michaelis showed a case of Internal Rotation Dislocation of the Shoulder. (To be published in *Journal of Bone and Joint Surgery*.)

sa communication devant l'Académie Impériale de Médecine, intitulée "De l'identité de l'état de rêve et de la folie" (1855) où, paraphrasant la définition de Kant: "Le fou est un dormeur éveillé", il concluait: "la folie est le rêve de l'homme éveillé", préluant ainsi aux études contemporaines sur les relations profondes et indissolubles de ces deux états. "J'avais vu dans le hachisch", écrit-il, "ou plutôt dans son action sur les facultés morales, un moyen puissant d'exploration en matière de pathologie mentale; je m'étais persuadé que, par lui, on devait pouvoir être initié au mystère de l'aliénation." Une observation récente et fortuite nous a suggéré qu'il y aurait peut-être intérêt à reprendre cette expérimentation. Il s'agissait d'un jeune homme de dix-huit ans qui, après avoir fumé une grande quantité de cigarettes qui contenaient, sans qu'il le sût, du hachisch, vécut une nuit d'onirisme et d'automatismes ambulatoires, au cours de laquelle il rêva qu'il assassinait son beau-père. Quand il se réveilla, loin du lieu où il s'était endormi, ce jeune Hamlet était tellement persuadé d'avoir commis ce crime qu'il alla se constituer prisonnier dans le plus proche commissariat de police en s'écriant: "Arrêtez-moi, je suis un assassin, je viens de tuer mon beau-père." L'enquête montra que celui-ci était en parfaite santé mais le pseudo-assassin, relâché par les policiers, devint un sujet d'observation pour les psychiatres qui découvrirent chez lui une névrose caractérielle, à base de complexe d'Edipe, que le hachisch avait brusquement révélée. Ainsi le hachisch peut-il dans certaines circonstances servir de révélateur des tendances latentes de la personnalité.

Après le hachisch, bien d'autres substances pharmacodynamiques furent employées dans le même but. Dès 1854, Morel utilisa l'éther pour explorer le psychisme des déments précoques; puis la cocaïne (Mantegazza, 1866), la mescaline (Heffter, 1894), la scopolamine (R. E. House, 1922), le scopochloralose (Baruk, 1933), suscitèrent de nombreux travaux. Chacune de ces drogues mériterait de longs développements mais, à l'heure actuelle, l'intérêt se concentre d'une part sur les barbituriques sodiques, agents de la narco-analyse, d'autre part sur les amines psychotoniques, agents du choc amphétaminique, et c'est sur la comparaison, voire l'association de leurs effets, qui sont dans une certaine mesure antagonistes, que je voudrais ici insister.

En 1930, Bleckwenn constata la disparition momentanée d'une stupeur catatonique après une injection intraveineuse d'amylal sodique. W. F. Lorenz, puis Lindeman, s'attachèrent aux explorations psychiques sous amylal sodique. A partir de 1936, le pentothal fut aussi employé avec succès et Stephen Horsley donna aux véritables psychanalyses chimiques facilitées par l'injection de ce produit le nom de *narco-analyse*, appliqué par la suite à toutes les analyses sous hypnose barbiturique. Chacun sait les résultats obtenus par cette méthode pendant la guerre de 1940-1945 par les psychiatres anglais et américains, tant dans le dépistage de la simulation que pour la guérison des névroses aiguës de combat. Les travaux de Sargant et Slater sur l'abréaction, ceux de Grinker et Spiegel sur la narco-synthèse, sont parmi les plus importantes acquisitions médicales de cette guerre.

Sous le nom générique de narco-analyse, on englobe à l'heure actuelle des techniques assez différentes mais qui reposent toutes sur le même critère nécessaire et suffisant: l'exploration du subconscient. La méthode réalise ce qu'en termes empruntés à Hughlings Jackson on peut appeler une dissolution de la conscience, c'est-à-dire un engourdissement de la vigilance semblable à celui de l'endormissement, et une libération de la subconscience, semblable à celle du rêve. Cette dissolution-libération comporte donc deux éléments, l'un négatif, l'autre positif, celui-ci étant la conséquence de celui-là. Elle clive dans une certaine mesure deux plans de l'activité mentale, l'un orienté vers l'action, l'autre vers le rêve, l'un qui répond aux synthèses mentales, l'autre aux automatismes psychologiques, l'un à la tension, l'autre à la détente, l'un enfin à l'organisation sociale et rationnelle de la personnalité, qui obéit aux exigences de l'utile, l'autre à l'organisation autistique et affective, apparemment désintéressée, qui obéit aux lois propres du dynamisme inconscient. Cependant dans le cadre de la narco-analyse, il convient de faire une différence entre la simple *subnarcose barbiturique*, au cours de laquelle le médecin ne joue qu'un rôle passif, laissant l'agent chimique produire son opération, et les *psychothérapies sous narcose*, au cours desquelles il joue un rôle actif. Tantôt il provoque le défoulement par l'interrogatoire, les associations dirigées, les tests, l'écriture automatique et le dessin automatique, voire le psychodrama et les play-technics; tantôt il explique la nature du lien entre les symptômes actuels et le conflit qui les conditionne, en facilite la synthèse et par là même le déconditionnement; tantôt il utilise la suggestibilité créée par la subnarcose pour essayer de réduire les symptômes par suggestion. Dans toutes ces éventualités la subnarcose n'est donc qu'une condition facilitante des psychothérapies, expressives, explicatives, ou suppressives.

Aussi bien chaque praticien peut-il introduire des modifications méthodologiques selon le but qu'il recherche. C'est ainsi que nous étant particulièrement attaché aux applications de la narco-analyse en médecine psycho-somatique, nous avons utilisé une technique de narco-analyse psycho-somatique, en explorant sous narcose non plus seulement les comportements verbaux mais encore les comportements somatiques, c'est-à-dire les gestes, les

useful in cases of depressive stupor for eliciting the depressive pattern of ideas; sodium amytal, by decreasing the anxiety, enables the patient to externalize these while methedrine, by increasing the anxiety, forces their production.

(2) *Schizophrenia*.—The presence or absence of catatonic features is important. These, when present, diminish in intensity with sodium amytal but become more marked with methedrine. When absent, methedrine may bring them to light, whereas sodium amytal has no such effect, but facilitates the contact with the patient. Psychological tests show likewise the different actions of these two drugs. Intellectual efficiency is decreased by methedrine but increased by sodium amytal, probably by the latter's action in reducing schizophrenic inhibitions. In the Rorschach test, with amytal, the responses are better organized, whereas methedrine not only increases the total number of responses and decreases the initial reaction time, but also brings out the schizophrenic nature of the protocol.

(3) *Acute neuroses*.—Methedrine is of value diagnostically but even more so therapeutically, its action being rapid and effective where emotional abreaction is the basis of cure. It appears to be particularly valuable in exploring thoughts already present in consciousness but not freely expressed: whereas sodium amytal is more effective in revealing unconscious forces and in relieving amnesic states. Given together the results are striking.

(4) *Chronic neurotic states*.—The therapeutic results here are not so good. Repeated sessions, with or without drug injections, are necessary, since the problem is the emotional re-education of the patient. Methedrine can only rarely be used, but through its "psychogogic action" it may be effective in externalizing conflicts where sodium amytal has failed. This is particularly true of psychasthenic states. There is, however, a risk of habit formation and addiction. Drug addiction can also be treated by combining methedrine and narco-analysis, methedrine being particularly useful in relieving the depressive symptoms resulting from the withdrawal of the addiction drug.

#### MEDICO-LEGAL ASPECT

One final, but important point must be made; these drugs should only be used for therapeutic ends and should on no account be used as part of medico-legal procedures.

### Sur les Explorations Pharmacodynamiques en Psychiatrie: Narco-analyse et Choc amphétaminique

#### I. — LES METHODES

Depuis l'antiquité on sait que certaines plantes et certains breuvages facilitent les aveux, rappellent des souvenirs oubliés, et rendent manifestes des tendances latentes de la personnalité. L'alcool, l'opium, le hachisch, le peyotl sont à la base de la plupart des philtres magiques utilisés sous des noms divers à tous les âges de l'histoire et sous toutes les latitudes géographiques. Breuvages sacrés du temple d'Epidaure, fumées enivrantes de la Pythie de Delphes, Népenthes dont il est fait mention dans Homère, Soma des brahmanes, Trag des Egyptiens, Al Khool, c'est-à-dire étymologiquement "le Subtil", des Arabes, Hachisch révélé à l'Occident par les récits de Marco Polo et des chroniqueurs des croisades. Peyotl des Indiens dont les premières relations des missionnaires nous racontent que "cette horrible mixture rend les païens incapables de tenir un secret", autant d'exemples de philtres à vertus psychologiques résumées dans le vieil adage latin, nuancé d'ironie: "in vino veritas."

L'application de ces notions à des explorations médico-psychologiques est de date relativement récente. Il n'y a guère plus d'un siècle en effet que Moreau de Tours publia son grand ouvrage "Du Hachisch et de l'Aliénation mentale" (1845). On s'intéressait alors beaucoup au hachisch et à Paris existait même un Club des Hachischins qui, en pleine Ile Saint-Louis, dans le vieil hôtel Pimodan, réunissait Baudelaire, Théophile Gautier, Daumier, Delacroix, et beaucoup d'artistes de leur temps. L'aliéniste, Moreau de Tours eut l'idée de se servir du hachisch pour l'étude de l'aliénation mentale. Après de multiples observations il conclut que le rêve du hachischin n'est pas seulement comparable mais identique au délire de l'aliéné, dont il reproduit en quelque sorte "l'expérience primaire". Ce fut là le point de départ de

à l'hôpital, le mutisme était complet et il était impossible d'obtenir de la malade le moindre renseignement. *Choc amphétaminique*: l'injection intraveineuse de trente milligrammes de méthédrine déclenche une agitation violente. La malade pleure, se tord sur son lit, s'accroche aux personnes qui l'entourent, s'écrie avec des gestes dramatiques: "Qu'ai-je fait? où est mon mari? où est mon enfant? J'ai tué mon petit. Ah! mon Dieu, j'ai fait du mal! Je l'ai tué d'un coup de rasoir. Je l'aimais bien pourtant." Ainsi, dans cette mélancolie stuporeuse la méthédrine a déclenché une bouffée anxieuse, à la faveur de laquelle la malade a extériorisé des idées délirantes de culpabilité et d'auto-accusation, puis elle est retombée dans son mutisme. *Subnarcose à l'amytal sodique*: disparition de l'anxiété, humeur sereine, sourires adéquats à des plaisanteries. La malade parle et expose aisément les motifs de sa tristesse récente. Elle sait qu'elle n'a pas tué son petit garçon et qu'il est en sécurité chez sa belle-mère. Ainsi, en même temps que la disparition de la douleur morale, il y a eu rectification des idées délirantes. Mais, au bout de quelques heures tout le syndrome mélancolique avait reparu.

Dans la *schizophrénie*, deux séries d'observations doivent être distinguées, selon qu'il y a ou non syndrome catatonique associé. Chez les schizophrènes avec catatonie, la catatonie cède à la subnarcose barbiturique qui permet alors d'en explorer les motivations psychologiques, elle s'aggrave et se complète après choc amphétaminique; le mutisme catatonique disparaît par l'amytal et se renforce par l'amphétamine. Chez les schizophrènes sans catatonie, l'amytal sodique permet un meilleur contact avec le malade, tandis que le choc amphétaminique peut faire apparaître la catatonie, ce qu'il ne fait pas chez un sujet normal, et rend plus apparente la dissociation mentale.

Voici à titre d'exemple un bref résumé de l'action antagoniste des psycholeptiques et des psychagogiques chez deux catatoniques. D., jeune homme de vingt ans, à antécédents schizophréniques, entre à l'hôpital avec un syndrome catatonique: mutisme complet, refus d'aliments, conservation des attitudes imposées, obéissance à des ordres absurdes, pas de flexibilité cireuse. *Subnarcose à l'amytal sodique*: cessation rapide de la raideur, de la conservation des attitudes, du refus d'aliments, du mutisme. Il déclare "qu'il s'est produit un changement dans son cerveau... il a l'esprit trop analytique, la synthèse lui manque... il est perdu avec la notion de temps". Il montre une grande difficulté à conduire un récit. Cependant il raconte avoir eu plusieurs expériences mystiques: "C'était une joie extraordinaire, inouïe, l'impression de saisir ce qui est fondamental, d'être en union directe avec Dieu." Et maintenant il sent que "la grâce lui a été reprise". L'état catatonique reprend au bout de quatre heures. *Choc amphétaminique*: apparition d'un blépharospasme rapide, hypersudation. Expérience délirante mystique: attitude extatique, expression de joie ineffable. Quelques rares paroles: "Je ressens une joie extraordinaire... une pureté... Dieu sauvera le monde". La conservation des attitudes s'accompagne de flexibilité cireuse et d'oppositionnisme. Bientôt mutisme complet et réapparition temporaire du refus d'aliments qui avait cessé depuis l'amytal.

D., jeune fille de vingt-cinq ans, a des troubles mentaux depuis l'âge de 19 ans. Fugues. Délire flou de structure paranoïde. Réponses à côté, barrages, persévérations idéiques, rationalisations purement verbales, impossibilité d'ordonner un discours et d'abstraire. Laconisme. *Choc amphétaminique*: 2': attitudes hiératiques, tête levée, air impassible et énigmatique; 4': mouvements respiratoires amples; 6': dévisage brusquement les assistants d'un air interrogateur et hautain. On lui demande quel a été l'effet de la piqûre: "comme vous voudrez, bien ou mal"; 10': se touche le cou alternativement à droite et à gauche avec des mouvements symétriques; 15': mutisme et opposition absolus; 20': se lève, exécute des mouvements lents et hypertoniques intermédiaires entre la danse et la gymnastique, echopraxie et obéissance automatique. L'après-midi: même attitude mais l'echopraxie est moins nette et l'obéissance automatique a fait place à l'oppositionnisme, mutisme persistant. *Subnarcose à l'amytal sodique*: disparition du mutisme et de tout l'aspect moteur du syndrome. Parle facilement. Bon contact affectif mais présente des troubles noétiques typiques. Interprète son attitude sous méthédrine comme des exercices de gymnastique.

Il est suggestif de comparer les résultats des tests obtenus dans l'état de subnarcose et après choc amphétaminique, chez les schizophrènes. Les tests d'efficiency témoignent d'une amélioration importante de l'efficiency sous l'effet du sodium amytal, sans doute due à l'action suppressive de l'amytal sur les inhibitions des schizophrènes (Layman); les résultats des tests de pensée conceptuelle sont inférieurs au cours d'un examen sous méthédrine à ceux de l'examen initial. Le test de Rorschach sous amytal montre des réponses plus faciles (Kelly) et mieux organisées (Layman); sous méthédrine nous avons constaté une augmentation habituelle du nombre des réponses, une diminution des temps de réaction mais une aggravation des signes schizophréniques qui deviennent évidents dans les cas où ils étaient peu caractéristiques sur le protocole pris dans des conditions normales.

Dans les *névroses*, nos recherches ont porté sur les névroses aiguës et sur les 1

attitudes, les expressions, les réactions viscérales, bref tout ce langage des organes qui plus que la parole est le véritable langage émotionnel. La reproduction expérimentale au cours de la subnarcoïse d'un symptôme somatique, par exemple une mimique, un tic, une crise nerveuse, une toux spasmodique, une dyspnée, une douleur précordiale ou abdominale, une sécrétion, une excrétion, dès que le cours des associations verbales évoque le conflit névrotique, constitue un véritable signal-symptôme, un indice psycho-somatique d'une réelle valeur quand on le retrouve identique, lors de séances successives, toujours le même chez un même malade.

En 1938, Hauschild, étudiant les amines sympathomimétiques et leurs isomères optiques, découvrit un nouveau corps, beaucoup plus puissant que la benzédrine de Berger et Dale et dont le chlorhydrate dextrogyre était doué d'un pouvoir psychotonique remarquable: il s'agissait de la méthylamphétamine, exactement phénylisopropyl-méthylamine, spécialisée en Allemagne sous le nom de Pervitin et en Angleterre sous celui de méthédrine. Il est remarquable que l'activité psychotonique soit spécialement fixée sur l'isomère droit, il s'agit là d'un nouvel exemple de l'importance fondamentale de la dissymétrie moléculaire, découverte par Pasteur, dans la chimie de la vie. Des études ultérieures entreprises non plus sur la phénylisopropylméthylamine mais sur la phénylisopropylamine ont également montré la considérable supériorité de l'action psychologique du composé dextrogyre sur le racémique: il semble plus de deux fois plus actif, ce qui arriverait si le lévogyre était complètement inerte.

L'action de la méthédrine est susceptible d'applications psychiatriques (Ivy et Goeltz, Simon et Taube, Sargant). Nous avons désigné sous le nom de choc amphétaminique (1947) les effets de l'injection intraveineuse de trente milligrammes de méthédrine: c'est bien effet d'un choc qu'il s'agit tant en est brutale l'action physique, manifestée en particulier par une hypertension artérielle avec élévation de la maxima de 4 à 5 cm. pendant une dizaine de minutes, et l'action psychique, faite d'une stimulation intellectuelle et émotionnelle, puissante et brève.

La comparaison des effets psychologiques des barbituriques sodiques et des amphétamines est d'autant plus intéressante qu'ils sont antagonistes. Les premiers ont une action déprimante sur le tonus psychique et émotionnel et entraînent une baisse de la tension psychologique; les seconds ont une action stimulante et entraînent une élévation de la tension psychologique. Plus précisément nous proposons de caractériser leurs actions respectives en disant que les premiers ont une action *psycholeptique* et les seconds une action *psychagogique*. La comparaison de leurs effets cliniques est utilement complétée par des batteries de tests: d'une part des tests d'efficiences, par exemple la Stanford-Revision du Binet-Simon, les form-boards, les tests moteurs (dextérité, tapping, etc.), d'autre part des tests de personnalité, par exemple le Rorschach et le Bernreuter, enfin des tests de suggestibilité, tel le press-release spécialement étudié par Eysenck et Rees.

Qui plus est, l'association, si paradoxale soit-elle, de ces médications psycholeptiques et psychagogiques est susceptible de donner des résultats intéressants; soit qu'on associe simplement l'ingestion per os de granules d'amphétamine (benzédrine) et d'amytal sodique, comme l'a fait Myerson; soit qu'on mette brusquement fin à la subnarcoïse créée par une injection intraveineuse d'amytal sodique, en faisant une injection intraveineuse de méthédrine.

## II. - LES RESULTATS

Nous ne retiendrons ici que les résultats les plus significatifs obtenus dans les psychoses et dans les névroses, aux fins de diagnostic ou de traitement.

Dans les *psychoses*, nos recherches ont porté sur deux maladies où le dérèglement de l'humeur s'opère en sens inverse: la maniaco-dépressive caractérisée par une hyperthymie, euphorique dans la manie, douloureuse dans la mélancolie, et la schizophrénie où s'observe un affaissement du tonus instinctivo-affectif de base: l'hypothymie.

Dans la *maniaco-dépressive*, l'état maniaque diminue ou disparaît transitoirement après injection d'amytal sodique, augmente après choc amphétaminique qui déclenche en général une explosion de joie maniaque et d'agitation; de même l'état mélancolique diminue ou disparaît transitoirement après injection d'amytal sodique qui exerce une action sédatrice sur la douleur morale, il augmente dans des proportions considérables après choc amphétaminique, ce qui peut avoir un réel intérêt pour le diagnostic des formes frustes et atypiques. La rupture d'un mutisme mélancolique, suivie de l'extériorisation verbale des thèmes de justification intellectuelle de l'état affectif, peut être obtenue par l'un ou par l'autre procédé, aussi bien par un psycholeptique, qui fait céder l'anxiété et exerce sur les inhibitions une action suspensive, que par un psychagogique qui augmente l'anxiété et exerce sur les inhibitions une action explosive: un résultat similaire est donc obtenu par deux mécanismes opposés.

Voici à titre d'exemple, brièvement résumée, l'une de ces observations de mutisme mélancolique. Il s'agissait d'une femme de quarante-deux ans, internée pour une mélancolie anxieuse avec mutisme et qui avait fait une tentative de suicide par coups de rasoir. A l'entrée

à l'hôpital, le mutisme était complet et il était impossible d'obtenir de la malade le moindre renseignement. *Choc amphétaminique*: l'injection intraveineuse de trente milligrammes de méthédrine déclenche une agitation violente. La malade pleure, se tord sur son lit, s'accroche aux personnes qui l'entourent, s'écrie avec des gestes dramatiques: "Qu'ai-je fait? où est mon mari? où est mon enfant? J'ai tué mon petit. Ah! mon Dieu, j'ai fait du mal! Je l'ai tué d'un coup de rasoir. Je l'aimais bien pourtant." Ainsi, dans cette mélancolie stuporeuse la méthédrine a déclenché une bouffée anxieuse, à la faveur de laquelle la malade a extériorisé des idées délirantes de culpabilité et d'auto-accusation, puis elle est retombée dans son mutisme. *Subnarcose à l'amytal sodique*: disparition de l'anxiété, humeur sereine, sourires adéquats à des plaisanteries. La malade parle et expose aisément les motifs de sa tristesse récente. Elle sait qu'elle n'a pas tué son petit garçon et qu'il est en sécurité chez sa belle-mère. Ainsi, en même temps que la disparition de la douleur morale, il y a eu rectification des idées délirantes. Mais, au bout de quelques heures tout le syndrome mélancolique avait reparu.

Dans la *schizophrénie*, deux séries d'observations doivent être distinguées, selon qu'il y a ou non syndrome catatonique associé. Chez les schizophrènes avec catatonie, la catatonie cède à la subnarcose barbiturique qui permet alors d'en explorer les motivations psychologiques, elle s'aggrave et se complète après choc amphétaminique; le mutisme catatonique disparaît par l'amytal et se renforce par l'amphétamine. Chez les schizophrènes sans catatonie, l'amytal sodique permet un meilleur contact avec le malade, tandis que le choc amphétaminique peut faire apparaître la catatonie, ce qu'il ne fait pas chez un sujet normal, et rend plus apparente la dissociation mentale.

Voici à titre d'exemple un bref résumé de l'action antagoniste des psycholeptiques et des psychagogiques chez deux catatoniques. D., jeune homme de vingt ans, à antécédents schizoïdes, entre à l'hôpital avec un syndrome catatonique: mutisme complet, refus d'aliments, conservation des attitudes imposées, obéissance à des ordres absurdes, pas de flexibilité cireuse. *Subnarcose à l'amytal sodique*: cessation rapide de la raideur, de la conservation des attitudes, du refus d'aliments, du mutisme. Il déclare "qu'il s'est produit un changement dans son cerveau... il a l'esprit trop analytique, la synthèse lui manque... il est perdu avec la notion de temps". Il montre une grande difficulté à conduire un récit. Cependant il raconte avoir eu plusieurs expériences mystiques: "C'était une joie extraordinaire, inouïe, l'impression de saisir ce qui est fondamental, d'être en union directe avec Dieu." Et maintenant il sent que "la grâce lui a été reprise". L'état catatonique reprend au bout de quatre heures. *Choc amphétaminique*: apparition d'un blépharospasme rapide, hypersudation. Expérience délirante mystique: attitude extatique, expression de joie ineffable. Quelques rares paroles: "Je ressens une joie extraordinaire... une pureté... Dieu sauvera le monde". La conservation des attitudes s'accompagne de flexibilité cireuse et d'oppositionnisme. Bientôt mutisme complet et réapparition temporaire du refus d'aliments qui avait cessé depuis l'amytal.

D., jeune fille de vingt-cinq ans, a des troubles mentaux depuis l'âge de 19 ans. Fugues. Délire flou de structure paranoïde. Réponses à côté, barrages, persévérations idéiques, rationalisations purement verbales, impossibilité d'ordonner un discours et d'abstraire. Laconisme. *Choc amphétaminique*: 2': attitudes hiératiques, tête levée, air impassible et énigmatique; 4': mouvements respiratoires amples; 6': dévisage brusquement les assistants d'un air interrogateur et hautain. On lui demande quel a été l'effet de la piqûre: "comme vous voudrez, bien ou mal"; 10': se touche le cou alternativement à droite et à gauche avec des mouvements symétriques; 15': mutisme et opposition absolus; 20': se lève, exécute des mouvements lents et hypertoniques intermédiaires entre la danse et la gymnastique, echopraxie et obéissance automatique. L'après-midi: même attitude mais l'echopraxie est moins nette et l'obéissance automatique a fait place à l'oppositionnisme, mutisme persistant. *Subnarcose à l'amytal sodique*: disparition du mutisme et de tout l'aspect moteur du syndrome. Parle facilement. Bon contact affectif mais présente des troubles noétiques typiques. Interprète son attitude sous méthédrine comme des exercices de gymnastique.

Il est suggestif de comparer les résultats des tests obtenus dans l'état de subnarcose et après choc amphétaminique, chez les schizophrènes. Les tests d'efficiences témoignent d'une amélioration importante de l'efficiences sous l'effet du sodium amytal, sans doute due à l'action suppressive de l'amytal sur les inhibitions des schizophrènes (Layman); les résultats des tests, de pensée conceptuelle sont inférieurs au cours d'un examen sous méthédrine à ceux de l'examen initial. Le test de Rorschach sous amytal montre des réponses plus faciles (Kelly) et mieux organisées (Layman); sous méthédrine nous avons constaté une augmentation habituelle du nombre des réponses, une diminution des temps de réaction mais une aggravation des signes schizophréniques qui deviennent évidents dans les cas où ils étaient peu caractéristiques sur le protocole pris dans des conditions normales.

Dans les *névroses*, nos recherches ont porté sur les névroses aiguës et sur les r



chroniques. L'emploi des épreuves psycholeptiques et psychagogiques n'y a plus seulement une valeur diagnostique mais une valeur thérapeutique.

Dans les névroses *aiguës*, qui succèdent à un traumatisme émotionnel, la narco-analyse seule ou associée au choc amphétaminique, constitue une méthode remarquable d'abréaction émotive. Elle guérit en quelques séances les amnésies d'origine affective et se montre efficace dans toute une série de manifestations psychiques et somatiques conditionnées par le refoulement des souvenirs traumatisants dont le dévouement avec réaction émotive engendre la guérison. Il est souvent difficile, dans ces névroses post-traumatiques, de faire la part du conscient et du subconscient, de la simulation et de l'hystérie, de la réticence et de l'amnésie. Sans qu'on puisse donner de règles formelles, il semble que la narco-analyse convienne mieux à l'exploration du subconscient et des amnésies et le choc amphétaminique à l'exploration du conscient et des réticences; quoi qu'il en soit, leur association constitue une méthode remarquable dans le traitement des névroses hystéro-traumatiques et des accidents pithiatiques avec sursimulation.

La guérison de ces névroses aiguës peut être obtenue dans des cas particulièrement heureux en une seule séance, même lorsque celle-ci est pratiquée longtemps après le début des troubles. C'est ainsi que Robert, vingt-neuf ans, fut guéri d'une amnésie traumatique et d'une contracture lombaire avec scoliose et plicature, durant depuis neuf ans, c'est-à-dire depuis l'explosion du navire de guerre à bord duquel il était marin. C'est ainsi que Denise, jeune fille de dix-neuf ans, fut guérie d'une dysphagie durant depuis deux ans, rapportée à tort à une sténose oesophagienne et traitée par gastrostomie; la guérison se produisit dès qu'elle eut revécu la scène traumatisante qui était à l'origine de sa dysphagie, à savoir l'irruption brutale de soldats allemands dans la ferme où elle était en train de prendre son repas.

Dans les névroses *chroniques*, dues au lent développement d'un complexe psychologique ancien qui a marqué toute l'évolution affective d'une personnalité, les méthodes pharmacodynamiques donnent des résultats beaucoup moins brillants. Néanmoins elles aident souvent à obtenir rapidement les clefs d'un conflit et peuvent même avoir une action thérapeutique. Mais il faut alors que les narco-analyses soient répétées et prolongées, et qu'elles comportent toute une gamme de psychothérapies sous narcoose associées à des séances de psychothérapies sans narcoose, où l'on veille à l'intégration progressive du matériel psychologique défilé. Il ne s'agit plus ici d'une délivrance quasi spontanée comme dans les névroses aiguës mais d'une maieutique qui exige toute une rééducation émotionnelle. Dans certaines névroses caractérielles et en particulier dans les névroses psychosomatiques, des cures durables peuvent être obtenues par la narco-analyse. L'emploi du choc amphétaminique ne saurait être ici qu'épisodique, cependant il est des cas où seuls les psychagogiques entraînent des extériorisations alors que les psycholeptiques n'ont aucun effet. Par exemple chez Thérèse, vingt ans, atteinte d'une grave névrose affective, ayant donné ses premières manifestations vers l'âge de quatorze ans et hospitalisée pour un état d'incertitude avec réticences allant jusqu'au mutisme, toutes les subnarcoses barbituriques échouèrent. La malade refusait de répondre et lorsqu'on insistait, renforçait son système de défense, déclarant avoir oublié jusqu'à son nom. Mais sous choc amphétaminique qui déclenchait une bouffée anxieuse très intense, le mutisme disparaissait et elle énumérait avec complaisance tous ses troubles. Plus tard, décrivant l'action de l'injection de méthédrine, elle disait: "La première fois que l'on m'a fait cette piqûre, je me suis sentie revivre. Je n'avais jamais été comme cela depuis l'âge de quatorze ans." L'effet durait environ quatre ou cinq heures après l'injection.

Cette action remarquable mais transitoire du choc amphétaminique est particulièrement nette dans les névroses de type neurasthénique et psychasthénique. La brusque élévation de la tension psychologique qu'il détermine, peut avoir pour effet de faire disparaître, en même temps que l'asthénie et son cortège somatique, les obsessions et les phobies. Mais ces effets, intéressants certes du point de vue de l'interprétation théorique de la neurasthénie de Beard et de la psychasthénie de Janet, font courir au malade qui les ont sur eux-mêmes constatés le risque d'accoutumance et de toxicomanie amphétaminique.

Par ailleurs, il convient de signaler que l'association des psycholeptiques et des psychagogiques peut être utile dans le traitement des névroses toxicomaniaques, la narco-analyse permettant d'en retrouver les origines psychologiques et les amines psychotoniques de supprimer les effets déprimants de la cure de désintoxication. Autant les barbituriques ont pris sur la composante anxieuse, autant les amphétamines sur la composante asthénique.

Si des techniques comme la narco-analyse et le choc amphétaminique, isolées ou associées, rendent de grands services dans le diagnostic des psychoses et le traitement des névroses, et plus généralement dans l'exploration pharmacodynamique de la personnalité, elles doivent néanmoins être strictement réservées à des fins médicales. En particulier, on n'imagine pas sans effroi que ces découvertes de la psycho-chimie puissent être mises à la disposition des polices. Il serait d'une cruelle ironie pour les médecins qui ont découvert ou préconisé ces méthodes afin de guérir, de voir utiliser aux fins d'asservissement de l'homme des expériences qu'ils n'ont faites qu'en vue de sa libération.

## Section of Medicine

President—Sir ADOLPHE ABRAHAMS, O.B.E., M.A., M.D., F.R.C.P.

[February 22, 1949]

### DISCUSSION ON PERIARTERITIS NODOSA

Dr. H. G. Miller: Periarteritis nodosa may be defined as a form of necrotizing inflammatory panarteritis affecting small and medium-sized arteries, accompanied both by signs of systemic infection and by focal symptoms due to the scattered primary arterial lesions and to the local circulatory disturbances varying from relative ischaemia to gross infarction, which these cause. It is not a very rare disease.

All the evidence suggests that periarteritis nodosa is an allergic response of anaphylactic type to a variety of antigenic agents usually, but not invariably, bacterial in nature. It must be admitted at once that even tentative recognition of the responsible antigen in a particular patient is the exception rather than the rule, but nevertheless the evidence for this view of the disease rests on a fairly firm basis. First, there is the tendency of the disease often to follow a recognized infection or drug intoxication. Secondly, the relative frequency in affected subjects of a past history of some disease such as acute rheumatism or asthma in which we believe hypersensitivity to be a factor; and the common occurrence during the course of periarteritis nodosa of symptoms in themselves recognized as allergic such as urticaria, asthma and nephritis. Thirdly, various experimental studies, in particular those of Rich (1942) and Rich and Gregory (1943) have shown that an acute necrotizing arteritis, similar to that of periarteritis nodosa, and sometimes accompanied by an acute carditis with Aschoff bodies, and by glomerulo-nephritis, can be provoked in rabbits by repeated injections of foreign serum—a syndrome analogous with human serum sickness.

In this view, periarteritis nodosa may be considered as a chronic recurrent urticaria of blood-vessels, in which repeated whealing of the vessel wall as part of an allergic vascular response of anaphylactic type leads ultimately to multiple focal necrosis of the wall of the artery, with breaches of medial continuity and reactive cellular infiltration. Rich has pointed out that this is exactly what happens in the tissues in the Arthus phenomenon, produced by repeated local injections of antigenic foreign serum, and another important link in this chain of evidence is found in the work of Bahrmann (1935) who produced a similar necrotizing arteritis in rabbits by repeated injections of histamine.

Amongst the conditions to which periarteritis nodosa seems to have been a sequel, pride of place must be given to a variety of streptococcal infections including tonsillitis, scarlet fever, erysipelas, glomerulo-nephritis and acute rheumatism. It is hardly surprising that periarteritis itself was at one time considered to be a streptococcal disease. However more rarely gonococcal and meningococcal infections, tuberculosis, syphilis, serum sickness and malaria have been recorded as antecedents. Amongst the non-bacterial antigens which seem to have played a similar role are several sulphonamides, organic arsenical preparations, thiourea, iodine, aspirin, epanutin, and desoxycorticosterone acetate. In my own experience arsenical intoxication, injection of foreign serum without recognizable serum sickness, pregnancy toxæmia, dental extraction, and apparently non-specific upper respiratory infections, have been related, in time at any rate, to the onset of the illness.

#### CLINICAL FEATURES

The difficulties of clinical diagnosis have, I believe, been too much stressed. It can, of course, be extremely difficult, but in a considerable proportion of cases the disease can be recognized with reasonable confidence even before pathological confirmation is obtained:

I recently saw a young man of 28 in the ward of a surgical colleague because of the onset of flitting polyarthritis with tachycardia, high fever and polymorphonuclear leucocytosis of 30,000.

chroniques. L'emploi des épreuves psycholeptiques et psychagogiques n'y a plus seulement une valeur diagnostique mais une valeur thérapeutique.

Dans les névroses *aiguës*, qui succèdent à un traumatisme émotionnel, la narco-analyse seule ou associée au choc amphétaminique, constitue une méthode remarquable d'abréaction émotive. Elle guérit en quelques séances les amnésies d'origine affective et se montre efficace dans toute une série de manifestations psychiques et somatiques conditionnées par le refoulement des souvenirs traumatisants dont le défolement avec réaction émotive engendre la guérison. Il est souvent difficile, dans ces névroses post-traumatiques, de faire la part du conscient et du subconscient, de la simulation et de l'hystérie, de la réticence et de l'amnésie. Sans qu'on puisse donner de règles formelles, il semble que la narco-analyse convienne mieux à l'exploration du subconscient et des amnésies et le choc amphétaminique à l'exploration du conscient et des réticences; quoi qu'il en soit, leur association constitue une méthode remarquable dans le traitement des névroses hystéro-traumatiques et des accidents pithiatiques avec sursimulation.

La guérison de ces névroses aiguës peut être obtenue dans des cas particulièrement heureux en une seule séance, même lorsque celle-ci est pratiquée longtemps après le début des troubles. C'est ainsi que Robert, vingt-neuf ans, fut guéri d'une amnésie traumatique et d'une contracture lombaire avec scoliose et plicature, durant depuis neuf ans, c'est-à-dire depuis l'explosion du navire de guerre à bord duquel il était marin. C'est ainsi que Denise, jeune fille de dix-neuf ans, fut guérie d'une dysphagie durant depuis deux ans, rapportée à tort à une sténose oesophagienne et traitée par gastrostomie: la guérison se produisit dès qu'elle eut revécu la scène traumatisante qui était à l'origine de sa dysphagie, à savoir l'irruption brutale de soldats allemands dans la ferme où elle était en train de prendre son repas.

Dans les névroses *chroniques*, dues au lent développement d'un complexe psychologique ancien qui a marqué toute l'évolution affective d'une personnalité, les méthodes pharmacodynamiques donnent des résultats beaucoup moins brillants. Néanmoins elles aident souvent à obtenir rapidement les clefs d'un conflit et peuvent même avoir une action thérapeutique. Mais il faut alors que les narco-analyses soient répétées et prolongées, et qu'elles comportent toute une gamme de psychothérapies sous narcose associées à des séances de psychothérapies sans narcose, où l'on veille à l'intégration progressive du matériel psychologique défoilé. Il ne s'agit plus ici d'une délivrance quasi spontanée comme dans les névroses aiguës mais d'une maieutique qui exige toute une rééducation émotionnelle. Dans certaines névroses caractérielles et en particulier dans les névroses psychosomatiques, des cures durables peuvent être obtenues par la narco-analyse. L'emploi du choc amphétaminique ne saurait être ici qu'épisodique, cependant il est des cas où seuls les psychagogiques entraînent des extériorisations alors que les psycholeptiques n'ont aucun effet. Par exemple chez Thérèse, vingt ans, atteinte d'une grave névrose affective, ayant donné ses premières manifestations vers l'âge de quatorze ans et hospitalisée pour un état d'inertie avec réticences allant jusqu'au mutisme, toutes les subnarcoses barbituriques échouèrent. La malade refusait de répondre et lorsqu'on insistait, renforçait son système de défense, déclarant avoir oublié jusqu'à son nom. Mais sous choc amphétaminique qui déclenchait une bouffée anxieuse très intense, le mutisme disparaissait et elle énumérait avec complaisance tous ses troubles. Plus tard, décrivant l'action de l'injection de méthédrine, elle disait: "La première fois que l'on m'a fait cette piqûre, je me suis sentie revivre. Je n'avais jamais été comme cela depuis l'âge de quatorze ans." L'effet durait environ quatre ou cinq heures après l'injection.

Cette action remarquable mais transitoire du choc amphétaminique est particulièrement nette dans les névroses de type neurasthénique et psychasthénique. La brusque élévation de la tension psychologique qu'il détermine, peut avoir pour effet de faire disparaître, en même temps que l'asthénie et son cortège somatique, les obsessions et les phobies. Mais ces effets, intéressants certes du point de vue de l'interprétation théorique de la neurasthénie de Beard et de la psychasthénie de Janet, font courir au malade qui les ont sur eux-mêmes constatés le risque d'accoutumance et de toxicomanie amphétaminique.

Par ailleurs, il convient de signaler que l'association des psycholeptiques et des psychagogiques peut être utile dans le traitement des névroses toxicomaniaques, la narco-analyse permettant d'en retrouver les origines psychologiques et les amines psychotoniques de supprimer les effets déprimants de la cure de désintoxication. Autant les barbituriques ont prise sur la composante anxieuse, autant les amphétamines sur la composante asthénique.

Si des techniques comme la narco-analyse et le choc amphétaminique, isolées ou associées, rendent de grands services dans le diagnostic des psychoses et le traitement des névroses, et plus généralement dans l'exploration pharmacodynamique de la personnalité, elles doivent néanmoins être strictement réservées à des fins médicales. En particulier, on n'imagine pas sans effroi que ces découvertes de la psycho-chimie puissent être mises à la disposition des policiers. Il serait d'une cruelle ironie pour les médecins qui ont découvert ou préconisé ces méthodes afin de guérir, de voir utiliser aux fins d'asservissement de l'homme des expériences qu'ils n'ont faites qu'en vue de sa libération.

clinical examination, occurring in more than 50% of cases, though the absent deep reflexes are often missed because they are not repeatedly looked for in such ill, cachectic patients, and are all too often dismissed as due to general weakness. Pathologically the kidneys are involved in about 90% of cases and *abnormal urinary findings* are very common indeed, being noted in at least two-thirds of recorded patients. The commonest finding is albuminuria, frequently constant, accompanied by casts in the urine, and attributed to nephritis; while hæmaturia is more often microscopic than gross, and may be persistent and also due to nephritis, or intermittent and arising from successive renal infarcts. *Hypertension* is found ultimately in about two-thirds of all cases and the blood-pressure often varies widely from reading to reading. Its relative rarity in the absence of urinary abnormalities and its high frequency where these are conspicuous, strongly suggest that it is usually renal in origin, and pathologically there can be no doubt of the high incidence of renal ischæmia in these patients. *Edema* occurs in about half the cases and may arise from polymyositis, nephritis, or congestive heart failure.

These then are the commonest clinical features—fever, tachycardia, raised sedimentation rate, polymorphonuclear leucocytosis, pain, wasting, and weakness, peripheral neuritis, urinary abnormalities, hypertension, and œdema.

In addition to these more general features, the focal symptoms which may be encountered in periarteritis nodosa are indeed legion. They may be completely absent, particularly in very acute cases, or they may occur in profusion. More often, however, a few of them occur in the individual patient. I will not weary you with a detailed account: no doubt there are many possible symptoms which have not yet been encountered, much less recorded. The nature and pathogenesis of most of them is clear from a consideration of the morbid anatomy of the disease.

#### PERIPHERAL NEURITIS IN PERIARTERITIS NODOSA

A consideration of periarteritis nodosa may throw light on the pathogenesis of infective polyneuritis in general, and its possible relationship to other diseases of which arteritis is a feature.

The peripheral neuritis of periarteritis nodosa may take one of three clinical forms. In the first and most characteristic there is a successive asymmetrical neuritis of individual nerve trunks: a mononeuritis multiplex, to my knowledge, closely simulated only by leprosy. In 1923 Wohlwill demonstrated its origin in obliterative endarteritis of the vasa nervorum. In the second form, a neuritis of this type is associated with the more usual form of symmetrical polyneuritis maximal in the lower limbs, quadriplegic in severe cases. In a typical case of my own, for instance, a severe left ulnar nerve lesion was associated with a mild polyneuritis limited to the legs. In the third and commonest type this familiar syndrome of symmetrical polyneuritis occurs alone. This last variety has in the past usually been attributed to toxic rather than to local ischæmic factors, but Dr. M. G. Nelson's careful examination of peripheral nerves at various levels in my own material leaves no doubt that endarteritis of the vessels to the nerves is the cause of this as of the mononeuritic type, and suggests that the nature of the lesion is probably determined by the localization and calibre of the vessels chiefly involved by the disease. In view of the great length of the axons involved—the longest in the body—it is not surprising that the nerves to the lower limbs are initially and maximally involved and that their function is early affected by the diffuse vascular insults which at the same time often involve the intimate vasculature of the whole of the peripheral nervous system.

There are of course several other forms of peripheral neuritis in which there is good reason to believe that the lesion is primarily vascular. It is of particular interest to recall that in serum sickness both neuritis of isolated nerves and typical symmetrical polyneuritis have been recorded, and that the latter may occasionally accompany severe urticaria. Although the patchy changes found in the peripheral nerves in advanced arteriosclerosis are usually clinically silent, there is little doubt that they too are ischæmic, while there is suggestive evidence also that the polyneuritis of porphyria arises as a sequel of vascular spasm and that arterial narrowing plays a considerable part in the neuropathies of exposure to cold and of diabetes.

There is singularly little to be found in the literature about the condition of the vasa nervorum in other forms of polyneuritis, but the clinically similar picture so often seen in cases of infective and post-infective polyneuritis raises the possibility that some of these also may arise on a basis of vascular allergy, and suggests the advisability of careful examination of the vasa nervorum in this wider range of material.

Finally I would like to discuss the possible relationship of periarteritis nodosa to temporal arteritis, and also to disseminated lupus erythematosus and related conditions.

cells per c.mm., beginning ten days after the complete relief of fairly acute abdominal pain by operative removal of a grossly normal appendix. The history, taken when I saw him, revealed that he had had eight months of cramps and tingling in the calves and feet with increasing difficulty in walking long distances, three months of frequent headaches and general ill-health, and two weeks of continuous fever prior to admission to hospital with his so-called "appendicitis". The finding of mild symmetrical polyneuritis limited to the lower limbs, a blood-pressure of 170/110, and albuminuria and microscopic hæmaturia quickly confirmed the initial clinical impression of periarteritis nodosa, which was strengthened by an equivocal but suspicious muscle biopsy, and later, unfortunately, confirmed at autopsy.

This straightforward case raises several useful points in clinical diagnosis. "Rheumatic Fever" occurring in a surgical ward always raises at any rate a suspicion of the disease, and the same applies to patients who develop severe abdominal pain during the course of acute rheumatism. This feature was stressed by Spiegel (1936) who speculated not unreasonably that the pain in some patients with so-called "abdominal rheumatism" might arise from the abdominal incidence of the acute arteritis which is a well-recognized pathological feature of severe acute rheumatism, and which seems to be analogous and indeed possibly identical in nature with the arteritis of early periarteritis nodosa. Another very suspicious feature illustrated in this case is the combination of marked hypertension, particularly in a young patient, with either sustained fever or polyneuritis. This patient's history illustrates also the frequency with which the diagnosis is missed because routine microscopic examination of specimens removed at operation is far from universal even in teaching hospitals. The surgeon's understandable reluctance to submit the slightly diseased or frankly normal appendix to pathological scrutiny may delay diagnosis for months. I have personally seen cases diagnosed from such specimens removed at appendicectomy, cholecystectomy, nephrectomy, and recently liver biopsy, while one of my present patients would undoubtedly have been correctly diagnosed twelve months ago if the subacutely swollen testicle removed early in his illness had been examined. Finally, and perhaps most important, this case serves to illustrate the rarity of several phenomena in the disease which have achieved notoriety out of proportion to their statistical frequency. Neither subcutaneous nodules nor eosinophilia occurs in more than 20% of cases and a family or past history of allergic illness is, in my experience, appreciably less frequent.

What then are the commonest features of diagnostic value?

First, *protracted fever with pronounced tachycardia*, which I would say is invariable at some stage in every case. Depending on the acuteness of the illness—and it may last for a few days only or for several years—the fever may be very high, or slight and grumbling. It is generally continuous, though it often becomes normal in remissions and usually in the healing phase. It rarely shows any response to salicylates, sulphonamides, penicillin or anti-histamine drugs, though occasionally chemotherapeutic agents or antibiotics do seem to influence the condition favourably. The response is rarely dramatic and it is difficult to be sure of it with a disease so capricious in its behaviour. Secondly, a *raised blood sedimentation rate* is rarely absent. This often gives a reading between 60 and 100 mm. (Westergren) in an hour, lasts long after the pyrexia has cleared up, and is, I think, a fair index of the activity of the pathological process. The blood also shows characteristically a high *polymorphonuclear-leucocytosis*, often of 20,000 or more. In one patient out of five, repeated counts will reveal a significant eosinophilia in an occasional film. Perhaps more frequent examinations would raise this proportion, but eosinophilia seems common only in patients with asthma or some other frankly allergic syndrome. With these blood findings is associated a moderate and slowly progressive secondary anaemia of ortho- or hypochromic type. Clinically these general signs of an infective process may be very puzzling, because exhaustive clinical and pathological investigation rarely reveals any significant local infective focus, and many of these cases are for long periods labelled "pyrexia of unknown origin". The most invariable subjective features are *pain, wasting and weakness*. Periarteritis nodosa is a very painful disease and in every case in my experience pain has been a striking and very often a presenting feature. It may arise from involvement of almost any body tissue, but one of the commonest forms is persisting severe abdominal pain, generalized or localized, arising from involvement of smooth muscle in the wall of a viscus or in the mesentery, and presenting a most difficult therapeutic problem in that it often continues for weeks or months and may respond imperfectly even to full dosage with morphia. Severe pain may arise also from arthritis which tends often to involve one or more large joints, and from painful polyneuritis or polymyositis with swollen, painful, and acutely tender muscles. Headache, angina, painful subcutaneous nodules, peripheral ischaemia of Raynaud type, and the acute pain of visceral infarction are much rarer. Wasting and weakness are generalized, and proportional to the acuteness of the process; and often also localized, due to peripheral neuritis, usually maximal in the lower limbs. The finding of peripheral neuritis, of which I shall have more to say later, is the most frequent major objective abnormality on

clinical examination, occurring in more than 50% of cases, though the absent deep reflexes are often missed because they are not repeatedly looked for in such ill, cachectic patients, and are all too often dismissed as due to general weakness. Pathologically the kidneys are involved in about 90% of cases and *abnormal urinary findings* are very common indeed, being noted in at least two-thirds of recorded patients. The commonest finding is albuminuria, frequently constant, accompanied by casts in the urine, and attributed to nephritis; while hæmaturia is more often microscopic than gross, and may be persistent and also due to nephritis, or intermittent and arising from successive renal infarcts. *Hypertension* is found ultimately in about two-thirds of all cases and the blood-pressure often varies widely from reading to reading. Its relative rarity in the absence of urinary abnormalities and its high frequency where these are conspicuous, strongly suggest that it is usually renal in origin, and pathologically there can be no doubt of the high incidence of renal ischæmia in these patients. *Œdema* occurs in about half the cases and may arise from polymyositis, nephritis, or congestive heart failure.

These then are the commonest clinical features—fever, tachycardia, raised sedimentation rate, polymorphonuclear leucocytosis, pain, wasting, and weakness, peripheral neuritis, urinary abnormalities, hypertension, and œdema.

In addition to these more general features, the focal symptoms which may be encountered in periarteritis nodosa are indeed legion. They may be completely absent, particularly in very acute cases, or they may occur in profusion. More often, however, a few of them occur in the individual patient. I will not weary you with a detailed account: no doubt there are many possible symptoms which have not yet been encountered, much less recorded. The nature and pathogenesis of most of them is clear from a consideration of the morbid anatomy of the disease.

#### PERIPHERAL NEURITIS IN PERIARTERITIS NODOSA

A consideration of periarteritis nodosa may throw light on the pathogenesis of infective polyneuritis in general, and its possible relationship to other diseases of which arteritis is a feature.

The peripheral neuritis of periarteritis nodosa may take one of three clinical forms. In the first and most characteristic there is a successive asymmetrical neuritis of individual nerve trunks: a mononeuritis multiplex, to my knowledge, closely simulated only by leprosy. In 1923 Wohlwill demonstrated its origin in obliterative endarteritis of the vasa nervorum. In the second form, a neuritis of this type is associated with the more usual form of symmetrical polyneuritis maximal in the lower limbs, quadriplegic in severe cases. In a typical case of my own, for instance, a severe left ulnar nerve lesion was associated with a mild polyneuritis limited to the legs. In the third and commonest type this familiar syndrome of symmetrical polyneuritis occurs alone. This last variety has in the past usually been attributed to toxic rather than to local ischæmic factors, but Dr. M. G. Nelson's careful examination of peripheral nerves at various levels in my own material leaves no doubt that endarteritis of the vessels to the nerves is the cause of this as of the mononeuritic type, and suggests that the nature of the lesion is probably determined by the localization and calibre of the vessels chiefly involved by the disease. In view of the great length of the axons involved—the longest in the body—it is not surprising that the nerves to the lower limbs are initially and maximally involved and that their function is early affected by the diffuse vascular insults which at the same time often involve the intimate vasculature of the whole of the peripheral nervous system.

There are of course several other forms of peripheral neuritis in which there is good reason to believe that the lesion is primarily vascular. It is of particular interest to recall that in serum sickness both neuritis of isolated nerves and typical symmetrical polyneuritis have been recorded, and that the latter may occasionally accompany severe urticaria. Although the patchy changes found in the peripheral nerves in advanced arteriosclerosis are usually clinically silent, there is little doubt that they too are ischæmic, while there is suggestive evidence also that the polyneuritis of porphyria arises as a sequel of vascular spasm and that arterial narrowing plays a considerable part in the neuropathies of exposure to cold and of diabetes.

There is singularly little to be found in the literature about the condition of the vasa nervorum in other forms of polyneuritis, but the clinically similar picture so often seen in cases of infective and post-infective polyneuritis raises the possibility that some of these also may arise on a basis of vascular allergy, and suggests the advisability of careful examination of the vasa nervorum in this wider range of material.

Finally I would like to discuss the possible relationship of periarteritis nodosa to temporal arteritis, and also to disseminated lupus erythematosus and related conditions.

cells per c.mm., beginning ten days after the complete relief of fairly acute abdominal pain by operative removal of a grossly normal appendix. The history, taken when I saw him, revealed that he had had eight months of cramps and tingling in the calves and feet with increasing difficulty in walking long distances, three months of frequent headaches and general ill-health, and two weeks of continuous fever prior to admission to hospital with his so-called "appendicitis". The finding of mild symmetrical polyneuritis limited to the lower limbs, a blood-pressure of 170/110, and albuminuria and microscopic hematuria quickly confirmed the initial clinical impression of periarteritis nodosa, which was strengthened by an equivocal but suspicious muscle biopsy, and later, unfortunately, confirmed at autopsy.

This straightforward case raises several useful points in clinical diagnosis. "Rheumatic Fever" occurring in a surgical ward always raises at any rate a suspicion of the disease, and the same applies to patients who develop severe abdominal pain during the course of acute rheumatism. This feature was stressed by Spiegel (1936) who speculated not unreasonably that the pain in some patients with so-called "abdominal rheumatism" might arise from the abdominal incidence of the acute arteritis which is a well-recognized pathological feature of severe acute rheumatism, and which seems to be analogous and indeed possibly identical in nature with the arteritis of early periarteritis nodosa. Another very suspicious feature illustrated in this case is the combination of marked hypertension, particularly in a young patient, with either sustained fever or polyneuritis. This patient's history illustrates also the frequency with which the diagnosis is missed because routine microscopic examination of specimens removed at operation is far from universal even in teaching hospitals. The surgeon's understandable reluctance to submit the slightly diseased or frankly normal appendix to pathological scrutiny may delay diagnosis for months. I have personally seen cases diagnosed from such specimens removed at appendicectomy, cholecystectomy, nephrectomy, and recently liver biopsy, while one of my present patients would undoubtedly have been correctly diagnosed twelve months ago if the subacutely swollen testicle removed early in his illness had been examined. Finally, and perhaps most important, this case serves to illustrate the rarity of several phenomena in the disease which have achieved notoriety out of proportion to their statistical frequency. Neither subcutaneous nodules nor eosinophilia occurs in more than 20% of cases and a family or past history of allergic illness is, in my experience, appreciably less frequent.

What then are the commonest features of diagnostic value?

First, *protracted fever with pronounced tachycardia*, which I would say is invariable at some stage in every case. Depending on the acuteness of the illness—and it may last for a few days only or for several years—the fever may be very high, or slight and grumbling. It is generally continuous, though it often becomes normal in remissions and usually in the healing phase. It rarely shows any response to salicylates, sulphonamides, penicillin or anti-histamine drugs, though occasionally chemotherapeutic agents or antibiotics do seem to influence the condition favourably. The response is rarely dramatic and it is difficult to be sure of it with a disease so capricious in its behaviour. Secondly, a *raised blood sedimentation rate* is rarely absent. This often gives a reading between 60 and 100 mm. (Westergren) in an hour, lasts long after the pyrexia has cleared up, and is, I think, a fair index of the activity of the pathological process. The blood also shows characteristically a high *polymorphonuclear-leucocytosis*, often of 20,000 or more. In one patient out of five, repeated counts will reveal a significant eosinophilia in an occasional film. Perhaps more frequent examinations would raise this proportion, but eosinophilia seems common only in patients with asthma or some other frankly allergic syndrome. With these blood findings is associated a *moderate and slowly progressive secondary anaemia of ortho- or hypochromic type*. Clinically these general signs of an infective process may be very puzzling, because exhaustive clinical and pathological investigation rarely reveals any significant local infective focus, and many of these cases are for long periods labelled "pyrexia of unknown origin". The most invariable subjective features are *pain, wasting and weakness*. Periarteritis nodosa is a very painful disease and in every case in my experience pain has been a striking and very often a presenting feature. It may arise from involvement of almost any body tissue, but one of the commonest forms is persisting severe abdominal pain, generalized or localized, arising from involvement of smooth muscle in the wall of a viscus or in the mesentery, and presenting a most difficult therapeutic problem in that it often continues for weeks or months and may respond imperfectly even to full dosage with morphia. Severe pain may arise also from arthritis which tends often to involve one or more large joints, and from painful polyneuritis or polymyositis with swollen, painful, and acutely tender muscles. Headache, angina, painful subcutaneous nodules, peripheral ischaemia of Raynaud type, and the acute pain of visceral infarction are much rarer. Wasting and weakness are generalized, and proportional to the acuteness of the process; and often also localized, due to peripheral neuritis, usually maximal in the lower limbs. The finding of peripheral neuritis, of which I shall have more to say later, is the most frequent major objective abnormality on

## TEMPORAL ARTERITIS

First, what is the relationship to periarteritis nodosa of so-called temporal arteritis? This condition was first described by Jonathan Hutchinson in 1890, rediscovered by Horton *et al.* (1932), and more recently and more accurately renamed cranial arteritis (Kilbourne and Wolff, 1946).

Horton's conception of temporal arteritis as a new and circumscribed clinical entity had to be materially modified when in typical cases widespread involvement was demonstrated first of other branches of the common carotid artery, secondly of the aorta and the larger arteries of limbs and brain, and thirdly, though admittedly to a strikingly lesser degree, of the intimate vasculature of the viscera. Finally, instances of pathologically identical cranial arteritis have been described in which the temporal arteries were spared.

The histopathological distinction of temporal arteritis from periarteritis nodosa was at first considered clear. Temporal arteritis was described as primarily adventitial, with absent or minimal cellular infiltration of the vessel wall, spreading axially, essentially less acute than periarteritis nodosa, not proceeding to nodule or aneurysm formation, without tissue or blood eosinophilia, and with a specific local giant-cell response. Subsequent studies have cast grave doubt on the validity of any such distinctions. The media is often involved in cranial arteritis, while periarteritis nodosa is not infrequently an equally indolent process in which nodule or aneurysm formation is often absent, eosinophilia by no means invariable and giant-cell formation not rare. Finally, temporal arteritis has been demonstrated in a typical case of periarteritis nodosa.

This is not to say that the two conditions are identical. The differences are, however, clinical rather than pathological, provisional rather than established, because there is not yet on record a sufficient number of cases of the much rarer cranial arteritis to provide a comprehensive catalogue of its manifestations. The real differences seem to be that cranial arteritis has never been recorded before late middle life (55 years) and secondly that in this condition the arteritis shows a predominant localization in the main branches of the aorta, with involvement of smaller peripheral and visceral arteries to a much slighter extent; an emphasis which is usually reversed in periarteritis nodosa.

The distinction of age-incidence is the more valid. After all, we know that periarteritis nodosa may be a remarkably localized process, highly selective in its incidence on parts of the arterial tree. Some of the cases showing marked neurological changes, for example, have had singularly little to show in other systems, while in other instances the vessels of the skin and subcutaneous tissues are quite disproportionately affected. The actual localization of the pathological changes in cranial arteritis is quite enough to account for many of its clinical differences from the graver disease—the rarity of visceral symptoms, urinary findings, and hypertension; and perhaps even for the good prognosis itself.

Final classification must await further information on aetiology, and we have less evidence as to the aetiology of cranial arteritis than of periarteritis nodosa, the only suggestion as to the possible nature of the former being offered by its frequent association with preceding infection of the nasopharynx, nasal sinuses, or teeth.

To the writer, the similarities of the two conditions are more striking than their differences, and it is difficult to believe that there is not a close relationship between them, but particularly in view of what appears to be the invariably favourable prognosis of cranial arteritis, a clinical distinction at any rate serves a useful purpose and is very well worth maintaining.

## DISSEMINATED LUPUS ERYTHEMATOSUS

Disseminated lupus erythematosus is an irregularly febrile systemic illness, acute, subacute or remittent, almost entirely limited to young women, nearly always ultimately fatal, and often but not essentially associated with the skin eruption which gives it its name. It is characterized by hyperglobulinemia with a high blood sedimentation rate, leucopenia, and a tendency to hæmaturia, involvement of serous and synovial membranes, and retinitis. Pathologically the commonest features are a diffuse arteritis histopathologically indistinguishable from that of periarteritis nodosa, a specific form of nephritis with "wire-loop" capillaries, and, in about one-third of all cases, verrucose endocarditis of Libman-Sacks type. These lesions are now widely considered to be due to diffuse fibrinoid destruction of the collagen ground-substance of the arterial walls and of other connective tissues, followed by secondary cellular infiltrations, and a considerable American literature has grown up around this and related "collagen vascular diseases" (Banks, 1941; Klemperer *et al.*, 1942; Stokes *et al.*, 1944; Baehr and Pollack, 1947; Rich, 1946-47). There can be no doubt that a similar pathological process seems to be locally or generally operative in a wide variety of clinically quite dissimilar conditions—disseminated lupus erythematosus, periarteritis nodosa, dermatomyositis and scleroderma, erythema nodosum, acute rheumatism, and glomerulonephritis. Some workers, including no less an authority than Arnold Rich, would include rheumatoid arthritis and thrombo-angiitis obliterans to this impressive list.



The similarity of the histopathological changes in the above conditions is beyond dispute, and there can be little doubt that many of their apparently great clinical differences are related to the distribution rather than the nature of the basic lesions. But histopathological identity does not necessarily imply identical aetiology, particularly in a tissue with a repertoire of pathological reactions as limited as that of collagen, and it must be admitted that there are pathological as well as clinical grounds for objection to a unitary theory of these diseases. Fibrinoid necrosis of collagen itself is certainly a reproducible feature of experimentally provoked hypersensitivity but it is also found locally in the vicinity of abscesses, ulcers and foreign bodies, and more generally in malignant hypertension and in experimental hypertension produced by Goldblatt clamps on the renal arteries. On clinical grounds, although disseminated lupus erythematosus often does succeed particularly streptococcal infections, and occasionally drug intoxications, and although it has on at least one occasion followed serum sickness, the role of allergy in this condition is less generally accepted and less well authenticated by experiment than is the case with periarteritis nodosa. Finally how does the unitary hypothesis of these diseases account for their obvious and profound clinical dissimilarities?

In my opinion none of these objections is fatal to the unitary conception of these diseases though particularly in the presence of ultimate ignorance as to aetiology this cannot perhaps yet be considered more than a stimulating hypothesis. There is certainly every justification for considering disseminated lupus erythematosus and periarteritis nodosa as separate clinical entities—yet the probability of a close family relationship between these conditions and with the larger group of collagen-vascular diseases seems to me much too great to be denied.

For example, I have at present under observation a girl of 19, who with an earlier history of two episodes of severe acute rheumatism, and following on many years of angioneurotic oedema with accompanying arthralgias, twelve months ago developed a skin eruption clinically identical with erythema nodosum, except for its wide distribution. Biopsy revealed that this arose on the basis of a diffuse arteritis and periarteritis and she proceeded to develop a mild polyneuritis. The skin nodules on one forearm became confluent and a brawny swelling developed clinically suggesting dermatomyositis, but, on biopsy, showing changes of diffuse collagenosis more characteristic of scleroderma. At the same time changing cardiac murmurs seemed to indicate the probability of a concurrent endocarditis. This girl is still under investigation; clinically she could be labelled as either periarteritis nodosa or as disseminated lupus erythematosus progressing to the phase of scleroderma. Pathologically she is certainly an instance of diffuse collagen-vascular disease.

This case illustrates well two points which Rich made in his Harvey Lecture—first, that these diseases show such similarities that differential diagnosis is often not only difficult but impossible; and secondly, that in any of them occasional features may be found which are usually supposed to belong to another member of the group.

If I am asked how the widely differing clinical manifestations of collagen-vascular disease could be accounted for I think there are three possible answers. First, *constitutional factors* may modify the expression of anaphylaxis as of other allergic phenomena. Exposed to a food allergen one subject develops asthma, one urticaria, and one nothing at all. Secondly, the *intensity and frequency of exposure to the antigen* are obviously factors to be considered. Thirdly, the *nature of the antigen itself* may play a part. In this connexion a piece of experimental work carried out in Boston in 1947 may prove to be the most important advance in this field since Rich's already classical experiments. Hawn and Janeway repeated Rich's experiments on rabbits, using crystalline bovine serum. Administration of crude serum or of the albumin fraction produced a necrotizing arteritis. When the gamma-globulin fraction alone was used the result was usually an acute glomerulo-nephritis sometimes with features suggestive of acute rheumatism.

Clinical and experimental observations such as these render it a not unduly fanciful hypothesis that this whole group of inflammatory-necrotizing lesions of blood-vessels, ranging possibly from anaphylactoid purpura of Henoch-Schönlein type at one end of the scale, to chronic periarteritis nodosa at the other, may ultimately prove to represent variants of a basic pattern of anaphylactic vasculitis.

#### REFERENCES

- BAEHR, G., and POLLACK, A. D. (1947) *J. Amer. med. Ass.*, 134, 1169.  
 BAHRMANN, E. (1935) *Virchows Arch.*, 296, 277.  
 BANKS, B. M. (1941) *New Engl. J. Med.*, 225, 433.  
 BOYD, L. (1940) *Bull. New York M. Coll., Flower and Fifth Ave. Hosps.*, 3, 32.  
 COOKE, W. T., CLOAKE, P. C. P., GOVAN, A. D. T., and COLBECK, J. C. (1946) *Quart. J. Med.*, N.S., 15, 47.  
 GORDON, L. Z., and THURBER, D. C. (1946) *Arch. Path.*, 42, 402.  
 GRANT, R. T. (1939-42) *Clin. Sci.*, 4, 245.  
 HAWN, C. V., and JANEWAY, C. A. (1947) *J. exp. Med.*, 85, 571.  
 HORTON, B. T., MAGATH T. B., and BROWN, G. E. (1932) *Proc. Mayo Clin.*, 7, 700.

- HUTCHINSON, JONATHAN (1890) *Arch. Surg.* (London), 1, 323.  
 KERNOHAN, J. W., and WOLTMAN, H. W. (1938) *Arch. Neurol. Psychiat.*, 39, 655.  
 KILBOURNE, E. D., and WOLFF, H. G. (1946) *Ann. intern. Med.*, 24, 1.  
 KLEMPERER, P., POLLACKS, A. D. and BAEHR, G. (1942) *J. Amer. med. Ass.* 119, 331.  
 LOGUE, R. B., and MULLINS, F. (1946) *Ann. intern. Med.* 24, 11.  
 MILLER, H. G., and DALEY, R. (1946) *Quart. J. Med., N.S.*, 15, 255.  
 RICH, A. R. (1942) *Bull. Johns Hopk. Hosp.*, 71, 123, 375.  
 — (1946-7) *Harvey Lect.*, 42, 106.  
 —, and GREGORY, J. E. (1943) *Bull. Johns Hopk. Hosp.*, 72, 65.  
 SAMPSON, R. S. (1945) *Brit. J. Ophthalm.*, 29, 282.  
 SPIEGEL, R. (1936) *Arch. intern. Med.*, 58, 993.  
 STOKES, J. H., BEERMAN, H., and INGRAHAM, N. R. (1944) *Amer. J. med. Sci.*, 207, 540.  
 WILSON, K. S., and ALEXANDER, H. L. (1945) *J. lab. Clin. Med.*, 30, 195.  
 WOHLWILL, F. (1923) *Firehows Arch.*, 246, 377.

**Professor R. J. Pulvertaft:** Morbid anatomists and histologists are becoming increasingly aware that periarteritis nodosa is neither so rare nor so fatal a disease as was believed only a few years ago. When the disorder presents with febrile albuminuria, eosinophilia and subcutaneous nodules it has indeed only to be thought of to be diagnosed. I have no experience of muscle biopsy, but in five personal cases, only one of which was fatal, the diagnosis was made during life by excision of a subcutaneous nodule.

Such nodules show an inflammatory process involving all the coats of a small or medium sized artery and extending well out into the adventitia. At post-mortem similar appearances may be seen, as in the first case illustrated, and shown by courtesy of Dr. A. D. Morgan (fig. 1). The patient was a West African negro who fell sick with a febrile disease when on a journey to Egypt, and was found to be suffering from malignant tertian malaria. He received a course of mepacrine treatment, but developed a left-sided paralysis, and died in fourteen days from pulmonary oedema. At post-mortem both kidneys showed infarction, and one was surrounded by a mass of coagulated blood. The section shown is from a small artery of the kidney, and illustrates well the periarterial reaction. The case is, however, of interest for two other reasons, first because periarteritis has been recorded in malaria, and secondly because the patient had been treated with a drug, mepacrine. There is ample clinical and some experimental evidence that this disease has often an allergic background, and that certain drugs, in particular the sulphonamides, are related to its development. When we find periarteritis complicating a disease, we must always consider whether the drug treatment of the primary disease may have been of aetiological significance.

At post-mortem, however, the histological picture is often one of arterial necrosis, with the formation of aneurysms, rather than of acute inflammation, and it is assumed that in this case we are dealing with a "burnt-out" disease. In addition thrombosis and intimal proliferation are very marked; I am not personally convinced that even at their earliest stages the vessels were truly inflamed, since the total duration of the fatal disease may be very short when such a picture is given.

Illustrations are given of such a case under the care of Sir Adolphe Abrahams, which has been reported by Dr. R. D. Tonkin, and myself. A young previously healthy woman presented as a case of uncontrollable vomiting following a drinking bout, but continued a classical and fatal course with eosinophilia, albuminuria and fits. The illustrations are of a branch of the left coronary artery, pancreas and kidney, showing aneurysmal formation in the coronary artery and intimal changes in the other vessels (figs. 2, 3, and 4).

The case illustrates the lack of inflammatory changes, and also the peculiar way in which the process is discontinuous, only isolated portions of one artery being affected. This is indeed a feature of all diseases of medium-sized arteries, as shown by the commonest peripheral arterial disease, medial sclerosis. Again it is not possible to exclude the possibility that the drug alcohol, or some other agent imbibed with the alcohol, may have been a precipitating factor in the development of the disease.

Without doubt the lesions of periarteritis may regress entirely. This is indicated by cases of complete clinical cure, when the diagnosis has been determined by the biopsy. I have, however, performed an autopsy on a case, confirmed by examination of one of a great number of subcutaneous nodules, and presenting as a case of multiple neuritis and muscular pain.

His nodules disappeared, but he was completely bed-ridden as a result of a protracted illness, and died, from no obvious cause, when his disease was clinically quiescent. Examination of all the viscera failed to show any evidence whatever of arterial disease: I could not establish any cause of death other than wasting and malnutrition.

The pathologist is often confronted with cases diagnosed clinically as malignant hypertension, but showing at post-mortem such extensive arterial and periarterial changes that the diagnosis of periarteritis is strongly suggested. I have seen such a case recently, a woman

of 61 admitted with pains in the calves of the legs and all the joints, and diagnosed as arthritis. After two months she became febrile, developed gross albuminuria and died of pulmonary oedema. While the renal lesions were typical of malignant hypertension, arteries in the spleen and uterus showed typical periarteritis.

The association of ocular symptoms with periarteritis, and with giant-cell arteritis which has for clinical and histological reasons been recognized by some authorities as a separate

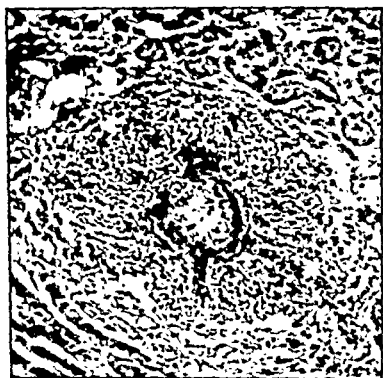


FIG. 1.—*Kidney*. From a case of malignant tertian malaria treated with mepacrine. Arterioles showing acute inflammatory changes.  $\times 72$ .



FIG. 2.—*Coronary artery*. Showing an aneurysm.  $\times 34$ .

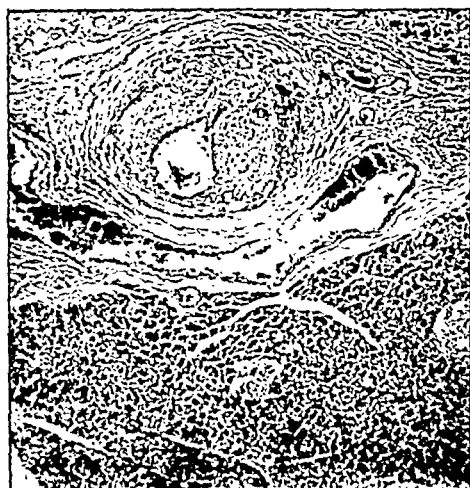


FIG. 3.—*Pancreas*. Showing marked intimal proliferation without inflammatory cells.  $\times 38$ .



FIG. 4.—*Kidney*. Showing intimal proliferation without inflammatory cells.  $\times 17$ .

entity, is well known, and I have observed periarteritis in the ciliary artery of a patient who became blind in the course of an attack of periarteritis, diagnosed by biopsy of a subcutaneous nodule; he survived. I would like, however, in conclusion to draw attention to a disease of some rarity, little mentioned in textbooks, but recognized by ophthalmic surgeons as "pseudo-tumour of the orbit". The patient presents with proptosis, but on operation sections show mainly inflammatory tissue.

My last illustrations are of such a case, a young man from Iceland with eosinophilia and

unilateral proptosis. A diagnosis of hydatid disease, once common in Iceland, but now rare, was not confirmed by intradermal or complement-deviation tests. A biopsy from the retro-orbital tissues showed only a non-specific inflammatory reaction (fig. 5).

While convalescing, the patient developed a subcutaneous nodule of the scalp at the margin of the hair over the involved eye. A biopsy of this lesion showed an inflammatory lesion related to small blood-vessels (fig. 6). The Wassermann reaction was negative.

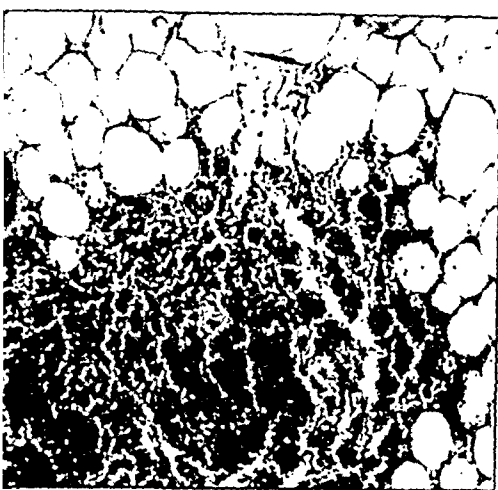


FIG. 5.—Post-orbital fat. Showing non-specific chronic inflammation.  $\times 86$ .

FIG. 6.—Nodule from scalp. Showing arterioles and related inflammatory cells.  $\times 86$ .

Admittedly the histological picture is equivocal, and consistent with many other disorders. It would, however, be worth while to investigate more fully cases of unilateral proptosis, to determine the frequency of eosinophilia and subcutaneous nodules, and to reconsider biopsies from the retro-orbital tissues in the expectation that a proportion of them may fall into the category of periarteritis.

**Professor Robert Platt:** I intend to devote my remarks almost wholly to the relation of periarteritis nodosa to renal and hypertensive disease, but I would first like to endorse Dr. Miller's opinion that the majority of cases can be diagnosed during life, because they show a recognizable clinical pattern. This consists of a rather prolonged illness characterized by irregular fever, leucocytosis and tachycardia. Blood cultures are obstinately negative and the temperature does not respond to penicillin. During the course of the illness certain episodes are liable to occur. These may take the form of atypical pneumonia or of acute abdominal pain, of rheumatic swellings, or of localized complications such as iritis or conjunctivitis. Sometimes there is cardiac pain or evidence of peripheral neuritis. If during an illness of this type albuminuria, renal failure or hypertension is discovered the diagnosis is almost certain. If on the other hand one looks for nodules and eosinophilia before committing oneself, a correct diagnosis of periarteritis nodosa will be made only once or twice in a lifetime.

There are four ways in which periarteritis nodosa may show evidence of renal or hypertensive disease: the first type is that in which albuminuria and uræmia are discovered rather unexpectedly in the course of a febrile illness such as I have described. I have seen several cases of this kind. One was a man aged 41 who was transferred to us from the Royal Eye Hospital where he had been admitted for iritis and conjunctivitis. He complained of pain in the limbs, the chest and the abdomen, which he had had at intervals for thirteen weeks. He had a persistently elevated temperature and appeared seriously ill. There were signs of a pleural effusion on the left side and there was slight swelling of the ankles. The blood-pressure was 140/80. There was a leucocytosis of 20,500 of which 72% were polymorphs and 3.8% eosinophils. The urine showed 1 gramme of albumin per litre and numerous pus cells, red cells and granular casts. A blood urea test was done and gave the surprising and unexpected figure of 458 mg. per 100 c.c. It should be noted that the blood-pressure was normal and that the illness bore no resemblance to nephritis. He died a few days after admission. Post-mortem examination showed periarteritis nodosa of the microscopic type

without aneurysm formation. I shall describe briefly later the type of renal lesion found in these cases.

The second type of case is that which presents itself as severe hypertension. Such a case was a man of 25 transferred to my Unit with a diagnosis of malignant hypertension. His blood-pressure was 215/160. There was bilateral papilloedema with retinal exudates. The urine contained albumin and the blood urea was 45 mg. per 100 c.c. We were suspicious of the diagnosis for several reasons; there was a leucocytosis of 19,500, there were occasional irregular rises of temperature, and there was a history of colicky abdominal pain. There was no family history of renal or hypertensive disease and I have personally never seen malignant essential hypertension at the age of 25. There were a few tender lymph-glands to be felt in the axillæ and groins. One of these and a small piece of artery were removed for biopsy with negative results. The patient's condition rapidly deteriorated, the blood urea rose to 222 mg. per 100 c.c., and he died a few weeks after admission. Post-mortem examination showed typical periarteritis nodosa of the macroscopic type with multiple aneurysms on the coronary, mesenteric and cystic arteries and in the liver, spleen and pancreas.

The third type is that in which the patient appears to have recovered from the initial illness but has been left with permanent hypertension; and the fourth type is that in which the clinical features of the case strongly resemble the rapidly progressive course of a Type I nephritis.

To illustrate this fourth type I would like to quote the case of a woman of 57 who was admitted to the Manchester Royal Infirmary in May of last year. She had suffered from asthma for many years and in September 1946 she had a retinal detachment apparently due to a slight blow on the head. While she was in hospital for this she had rheumatic pains in the ankles and knees. On returning home from the hospital she noticed swelling of the legs which lasted for a few weeks, and she developed frequent headaches. In March 1948 she developed a sore throat followed by some rheumatic pains, and a fortnight later by swelling of the face and legs, headache and hæmaturia. When first admitted the urine contained blood and albumin and the blood-pressure was 200/105. There was occasional œdema of the legs and back. Irregular pyrexia continued during the whole of the illness and there was an episode of what appeared to be bronchopneumonia which did not respond to penicillin. In June pericardial friction was noticed and persisted until the end. At times there were severe attacks of asthma. The urine contained albumin throughout, and there was an increasing anæmia with a leucocytosis varying from 18,000 to 23,000. The blood urea was 72 mg. per 100 c.c. on admission and gradually rose to 360 mg. before she died. During the illness periarteritis nodosa was considered because of the association with asthma and the episodes of rheumatism and bronchopneumonia. The pyrexia and the rapid progress, moreover, were unlike most cases of nephritis. Post-mortem examination showed a renal condition which was consistent both macro- and microscopically with a diagnosis of Type I nephritis of the rapidly progressive variety, but vessels of the liver, pancreas, and small intestine showed lesions of periarteritis nodosa. In cases like this it seems almost impossible and probably illogical to draw an absolute distinction between the two conditions.

*Pathology.*—I will again keep my remarks mainly to the kidney. The microscopic type of periarteritis nodosa in which no gross changes are found at the post-mortem is probably considerably commoner than the classical or aneurysmal type. Periarteritis nodosa may therefore easily be overlooked unless the pathologist is aware of its importance and its peculiarities. The presence of multiple infarcts without obvious cause is a finding at post-mortem that should arouse suspicion. Although the lesions are widespread they occur irregularly in a number of organs and it is essential to examine many sections of tissue from many places. The essential lesion is acute fibrinoid necrosis of part of a vessel wall with perivascular cellular infiltration. Arteries of medium or small size are commonly involved, but arterioles and capillaries may be involved as well. The lesion is often segmental and leads to partial loss of the internal elastic layer, which may be an important clue to lesions which have healed. Weakness of the arterial wall may lead to aneurysm formation, and thrombosis of the vessel may lead to infarcts in organs such as the spleen, kidney, and liver. My colleagues, Davson and Ball, in a study of the pathology of the kidney in periarteritis nodosa in a recent joint paper (1948) divide the cases into two groups. In the first group the important lesion is a patchy fibrinoid necrosis of the glomerular tufts with a variable amount of crescent formation and fibrosis. Quite often there is periglomerular cellular infiltration giving rise to the "explosive" appearance described by Ellis (1942) in rapidly progressive cases of Type I nephritis. Some of his cases we think may have been periarteritis nodosa of this type. Our evidence for thinking that this glomerular lesion is typical of periarteritis nodosa is based on the finding of arteries in the kidney and other organs in these cases which showed typical periarteritis nodosa. Sometimes these arterial lesions could not be

found in the kidney itself although the glomerular lesion was widespread. All our cases of this kind were of the microscopic type without aneurysm formation. Clinically they were fairly uniform in having the febrile illness I have described with a rather unexpected discovery of albuminuria with termination in uræmia without hypertension. Davson and Ball believe that the glomerular lesion is specific and distinguishable from that of Type I nephritis, malignant hypertension, or focal embolic nephritis.

(Slides were shown to illustrate the lesions described.)

The second pathological group was more varied. There were no widespread glomerular necrotic lesions but the renal vessels showed either periarteritis nodosa or periarteritis nodosa and malignant hypertension combined. Clinically many of these cases had run the course of severe hypertension of malignant type. In some of them the periarteritis nodosa lesions in the larger renal arteries could well have been a cause of renal ischæmia, and we suggest that this is the initial cause of the hypertension and that in some cases a vicious circle is established, the hypertension progressing to a malignant termination with characteristic arteriolar lesions superimposed on the original pattern of periarteritis nodosa.

I have pointed out that in some cases it seems artificial to distinguish between periarteritis nodosa and Type I nephritis. In other cases the course and pathology are sharply distinct. At the other end periarteritis nodosa merges into disseminated lupus, and perhaps into rheumatic fever and rheumatoid arthritis, as Rich (1946) has suggested, and in all these conditions fibrinoid necrosis with perivascular infarcts of arteries may be encountered. Probably the whole group belongs to the anaphylactic diseases but at present it still seems desirable, if only for the practical reasons of study and prognosis, to differentiate between the members of the group provided that by doing so we do not close our minds to a wider concept of their pathology.

#### REFERENCES

- DAVSON, J., BALL, J., and PLATT, R. (1948) *Quart. J. Med. N.S.*, **17**, 175.  
ELLIS, A. (1942) *Lancet* (i), 1.  
RICH, A. R. (1946-47) *Harvey Lect.*, **42**, 106.

Dr. H. G. Miller, in reply to the discussion on his paper, said: Perhaps the increasing armamentarium of drugs, as well as more frequent clinical and pathological recognition of the disease, may be partly responsible for the apparent increase in its incidence. With regard to the healed disease, it may certainly like active periarteritis nodosa be missed at autopsy, and it can prove fatal from, for example, the effects of renal or cardiac ischæmia. I am unfamiliar with eosinophilic proptosis, but there is every reason to believe that localized and abortive forms of periarteritis—"formes frustes"—are not at all infrequent and there is nothing inherently improbable in such a relationship in this instance. I agree that leucopenia is a fairly constant feature of disseminated lupus erythematosus and rare in periarteritis nodosa. It is interesting to note that in the case of the young girl described above the white count was 10-12,000 per c.mm. with up to 6% of eosinophils. Pathologically as well as clinically her case seems to fall midway between the two diseases. As regards muscle biopsy I have had several positive results in the absence of nodules, and have usually, but not invariably, been able to take the specimen from an area of muscle tenderness.

## Clinical Section

President—G. E. VILVANDRÉ

[February 11, 1949]

### Three Children Successfully Operated Upon for Congenital Atresia of the Œsophagus with Œsophago-tracheal Fistula.—R. H. FRANKLIN, F.R.C.S.

(I) Jennifer S., born 10.1.47. Birth-weight 7 lb. 7 oz. Referred by Professor Alan Moncrieff.

13.1.47: Extrapleural operation. Ligature and division of fistula. Reconstruction of Œsophagus.

19.1.47: Kader-Senn gastrostomy.

31.1.47: Gastrostomy tube removed.

(II) Bridget M., born 24.4.47, by Cæsarean section. Birth-weight 6 lb. 7 oz. Referred by Miss M. D. Daley, M.D., F.R.C.O.G.

26.4.47: Extrapleural operation as in Case I.

Uninterrupted recovery. Gastrostomy was not required.

(III) Paul D. F. T., born 14.2.48. Referred by J. D. Younghusband, F.R.C.S.

18.2.48: Extrapleural operation as in Cases I and II. Uninterrupted recovery. Gastrostomy was not required.

The third patient of this series has just recovered from an attack of measles and is making good progress. All three children are taking ordinary diet and putting on weight like any other child of their age.

These three children are the only published successes in this country.

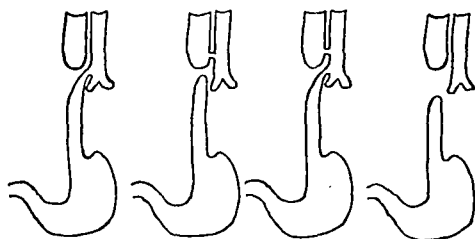
*Comment.*—Congenital atresia of the Œsophagus was first described in 1697 by Gibson who was a grandson of Oliver Cromwell, and Physician-General to the Army.

Some 250 years elapsed before a success was recorded in the management of the condition. MacKenzie collected records of 43 cases in 1884, and in 1910 Sir Arthur Keith found 14 examples of atresia in the museums of London.

Treatment was neglected because the condition was seldom diagnosed during life and there has been a popular belief that not only is the condition one of extreme rarity, but it is commonly associated with other congenital lesions of an equally serious nature.

At the Postgraduate Medical School of London four cases of atresia were found in 10,543 deliveries (1 in 2,635 deliveries).

Although the possibility of other abnormalities, particularly imperforate anus, must be kept in mind it is encouraging to note that in 45 consecutive cases Cameron Haight found only one patient with an additional deformity which was incompatible with life.



Type IIIb 80%; Type IIIa; Type IIIc; Type II.  
FIG. 1.—Types of Œsophageal atresia.

The characteristic lesion is an atresia: the upper Œsophageal segment ending blindly at about the level of the vena azygos arch, and the lower segment arising as a fistula from the back of the trachea within one centimetre of the bifurcation. This type accounts for 80% of the cases (fig 1).

found in the kidney itself although the glomerular lesion was widespread. All our cases of this kind were of the microscopic type without aneurysm formation. Clinically they were fairly uniform in having the febrile illness I have described with a rather unexpected discovery of albuminuria with termination in uræmia without hypertension. Davson and Ball believe that the glomerular lesion is specific and distinguishable from that of Type I nephritis, malignant hypertension, or focal embolic nephritis.

(Slides were shown to illustrate the lesions described.)

The second pathological group was more varied. There were no widespread glomerular necrotic lesions but the renal vessels showed either periarteritis nodosa or periarteritis nodosa and malignant hypertension combined. Clinically many of these cases had run the course of severe hypertension of malignant type. In some of them the periarteritis nodosa lesions in the larger renal arteries could well have been a cause of renal ischemia, and we suggest that this is the initial cause of the hypertension and that in some cases a vicious circle is established, the hypertension progressing to a malignant termination with characteristic arteriolar lesions superimposed on the original pattern of periarteritis nodosa.

I have pointed out that in some cases it seems artificial to distinguish between periarteritis nodosa and Type I nephritis. In other cases the course and pathology are sharply distinct. At the other end periarteritis nodosa merges into disseminated lupus, and perhaps into rheumatic fever and rheumatoid arthritis, as Rich (1946) has suggested, and in all these conditions fibrinoid necrosis with perivascular infarcts of arteries may be encountered. Probably the whole group belongs to the anaphylactic diseases but at present it still seems desirable, if only for the practical reasons of study and prognosis, to differentiate between the members of the group provided that by doing so we do not close our minds to a wider concept of their pathology.

#### REFERENCES

- DAVSON, J., BALL, J., and PLATT, R. (1948) *Quart. J. Med. N.S.*, 17, 175.  
ELLIS, A. (1942) *Lancet* (i), 1.  
RICH, A. R. (1946-47) *Harvey Lect.*, 42, 106.

Dr. H. G. Miller, in reply to the discussion on his paper, said: Perhaps the increasing armamentarium of drugs, as well as more frequent clinical and pathological recognition of the disease, may be partly responsible for the apparent increase in its incidence. With regard to the healed disease, it may certainly like active periarteritis nodosa be missed at autopsy, and it can prove fatal from, for example, the effects of renal or cardiac ischemia. I am unfamiliar with eosinophilic proptosis, but there is every reason to believe that localized and abortive forms of periarteritis—"formes frustes"—are not at all infrequent and there is nothing inherently improbable in such a relationship in this instance. I agree that leucopenia is a fairly constant feature of disseminated lupus erythematosus and rare in periarteritis nodosa. It is interesting to note that in the case of the young girl described above the white count was 10-12,000 per c.mm. with up to 6% of eosinophils. Pathologically as well as clinically her case seems to fall midway between the two diseases. As regards muscle biopsy I have had several positive results in the absence of nodules, and have usually, but not invariably, been able to take the specimen from an area of muscle tenderness.



than five and a half days. Of these 4 further cases attempted by this approach 3 were under-weight premature infants and in all an undue length of time had elapsed before the diagnosis was made.

I carried out the extrapleural approach on the stillborn and was impressed by the difficulty of the operation.

My view of the relative merits of the two approaches was modified by the first completely successful anastomosis carried out by Haight in 1941. This early success was repeated by Haight, Ladd and others—all by the extrapleural route. This was the method used in the three children, Cases I, II and III (fig. 2).

Mr. R. H. R. Belsey has operated on 3 children by the transpleural route and one of them, who was born round about Christmas, is making good progress. It may be that penicillin, which was not available in the early cases, has made the transpleural route safer, but I do not feel disposed to discard the extrapleural operation which has given such excellent results, in spite of its difficulty, until further information is available on this point.

*Diagnosis.*—All who have the care of newborn infants, particularly midwives, should be taught to look for the early signs of congenital atresia.

Excess of mucus in the nasopharynx occurs in normal infants but aspiration soon relieves any cyanosis which may have been present. Recurrent cyanosis, exaggerated by any attempt at feeding and accompanied by spluttering and choking and the appearance of frothy mucus usually indicates œsophageal atresia.

An infant suffering from atresia is usually avid for its feed and sucks strongly, only to be overwhelmed by one of these attacks.



FIG. 3.—An X-ray taken after iodized oil had been given before it was realized how necessary it is to avoid the medium spilling over into the trachea.



FIG. 4.—A good X-ray in which the iodized oil has been introduced cautiously by a catheter into the upper segment. Note that there is no spill-over into the lungs.

Once the suspicion of atresia has been raised all feeds must be stopped and aspiration carried out frequently. A well-lubricated rubber catheter passed through the mouth will be held up 10–12 cm. from the alveolar margin in the case of atresia. Care must be taken that too fine a catheter is not used, as this may curl up in the blind segment and give rise to the erroneous conclusion that the œsophagus is normal.

Confirmation is made by radiological examination. Great care is essential and the procedure should be as follows:

- (1) The infant is screened and the state of the lungs determined.
- (2) The stomach and intestines are examined for air. If air is present in a case of atresia a fistula must be present between the lower segment and the trachea.
- (3) 1 c.c. of iodized oil is injected through the catheter and its course followed. If it fills the bottom of the blind upper segment it is left in position for a minu

The next type most often found is that in which both upper and lower segments end blindly without any fistulous communication with the trachea. Unusual types occur in which there is a communication between the upper segment and the trachea or between both segments and the trachea.

Cameron Haight has described one case in which a fistula was found communicating with an œsophagus which was otherwise normal. Dr. O'Reilly has a specimen which shows a cleft-like defect extending up to the larynx and which may, I think, be regarded as an exaggerated form of the single case described by Cameron Haight.

Early attempts at operation failed because the true nature of the deformity was not understood. If a gastrostomy was carried out the feed passed up into the lungs with disastrous results. Even in those cases in which no fistula was present the blind upper segment filled up with mucus and spilled over into the trachea.

With the knowledge of all the past failures at treatment Professor Grey Turner urged me to try the effect of passing a strong silk ligature around the cardia and at the same time to carry out a gastrostomy.

This method had been used unsuccessfully before, but we thought that failure may have followed because the necessity of keeping the upper segment empty had not been recognized. An opportunity presented itself on November 21, 1938, in a male child (birth-weight 6 lb. 7 oz.) who was 72 hours old at the time of the operation.

He survived the operation for seven days, by the end of which time the ligature had cut through the cardia and re-established the fistula.

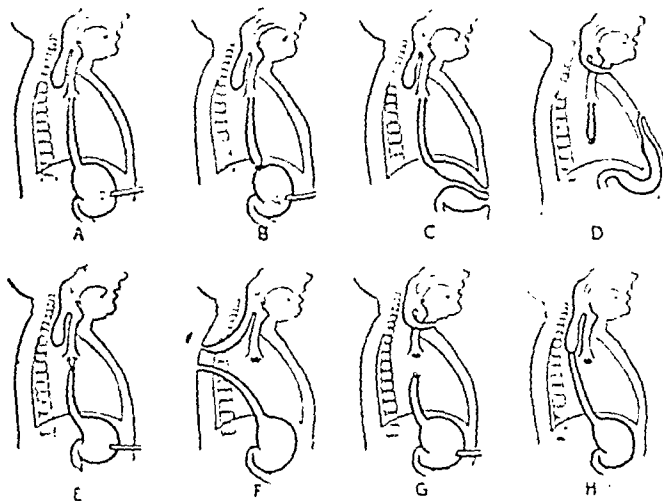


FIG. 2.—Diagrams to show various types of procedure. Upper line: Primarily abdominal procedures. A.—Gastrostomy. B.—Gastrostomy and abdominal ligation of œsophagus. C.—Transection of stomach. D.—Cervical œsophagostomy and transplantation of cardia. Lower line: Primarily thoracic procedures. E.—Mediastinal ligation and gastrostomy. F.—Mediastinal ligation and transplantation of lower segment (cervical œsophagostomy). G.—Mediastinal ligation, cervical œsophagostomy and gastrostomy. H.—Direct anastomosis. (From Humphreys, *Surg.*, 1944, 15, 812, with acknowledgments to the Author and C. V. Mosby Co., St. Louis.)

Further discussions led to the determination to try a direct approach on the next occasion. This did not arrive until 16.10.41 when a transpleural operation with reconstruction of the œsophagus was completed in a child 84 hours old and who weighed 4 lb. 5 oz. at birth. This child lived only seventeen hours but it proved that the operation was not only possible but did not appear to produce undue shock. Meanwhile Ladd in 1939 and Leven in 1940 produced successful results from staged operation. The multiplicity of operations required and the fact that a normal œsophagus was not attained at the end of it all encouraged me to continue the transpleural approach with anastomosis where possible. None of the cases survived longer

**Professor G. Grey Turner:** Only a few years ago it was thought that congenital atresia of the oesophagus was something beyond the scope of effective treatment of any sort. I can vividly remember an occasion which convinced me that we really must attempt something more for the relief of these doomed infants and that effective intervention would probably mean a direct attack at the site of the anomaly itself, in fact exactly what has turned out to be the proper method of dealing with the anomaly. It was in Glasgow in December 1936: I had been lecturing on the oesophagus and was afterwards invited to inspect some pathological treasures which had been retrieved from the wonderful purges of the Children's Hospital in that City. I was expecting to find perhaps two or three rather odd specimens of congenital anomalies of the oesophagus but instead a large bucketful of all types was produced for my examination. I was immensely impressed with the care that had been displayed by the late Brown Kelly in going into the pathological features of these conditions with the assistance of his friend, Professor Blacklock. It was that experience which made me realize that the condition might be much more frequent than had been supposed and that it was not just an interesting curiosity. The oesophageal anomaly in the nature of atresia probably occurs in about 1:3,000 births but as most of the infants die of pneumonia the actual condition is not suspected nor is it disclosed at autopsy unless particularly looked for. After seeing this wealth of material at Glasgow I was convinced that we must devise a direct intervention at the site of the atresia and probably by the posterior oesophageal route (see Grey Turner, G., 1938, *Brit. med. J.* (ii), 1110). Such an exposure was tried on a couple of stillborn infants and one also studied the problem in transverse sections of infantivers. These observations convinced me of the practicability of the proposed intervention while emphasizing the difficulties, due to the extreme smallness and delicacy of the parts concerned. The opportunity to try the operation did not occur until the first case on which Mr. Franklin operated at my suggestion at the Postgraduate School in October of 1941. The delay was partly due to the fact that we had to depend on receiving our patients from the Maternity Department and partly because our efforts were distracted by other preoccupations in connexion with the late war. Incidentally, one or two experiences arising from bombing raids convinced me of the remarkable relative capacity of infants of tender age and encouraged me to proceed with the major interference contemplated. It was about that time, when discussing the problem in the presence of our very some American visitors, that I learned for the first time that an American surgeon, Dr. C. Haight, already operated with success in at least one case of atresia, though the case was not published three years later (Haight, C., and Townsley, H. A. 1943, *Surg. Gynec. Obstet.*, 76, 672). Living further into the history has disclosed that very occasional attempts at direct intervention have been made since Richter was bold enough to make the suggestion as long ago as 1913. Even I do not think a sufficient number of these cases come before the surgeon at the proper time and I believe that we still require to carry on propaganda among obstetricians, maternity nurses, midwives and even paediatricians directed to their early recognition. If surgical intervention is to be attended by a reasonable chance of success, it must be carried out before secondary pneumonic changes have taken place and that probably means within about forty-eight hours after birth. In connexion with the early diagnosis, I want to say a word about the avidity with which these little infants attempt to take food and with the striking cyanosis and accumulation of mucus which usually attends their efforts to swallow. So far as the actual operative interference is concerned, I would stress the wisdom of being ready prepared and of being furnished with suitable instruments and, for this purpose, I think that the instruments ordinarily used for cleft palate operations will probably be found to be most useful, especially long delicate forceps, fine needles and suitable reliable needle holders on long handles. Very fine tantalum wire may prove to be the best suture material. In suturing a tube such as the infants' oesophagus I would utter a warning as to the need for very great care not to inadvertently make a stricture. Things should be so arranged that when the suturing is completed the lumen at the site is bigger than at other parts of the tube. To this end I should be inclined to advise that we should not attempt to use a single suture carried all round but that we should use either a series of interrupted sutures or an encircling stitch that is interrupted in such a way that only about a third of the tube is included in any one thread. Those who have had the most experience must lay down dicta for the guidance of the meeting but I should feel that it is probably more in the safety of the operation to provide a track to the surface from near the site of the atresia, so that if leakage does occur fluids can freely escape externally and will not be spread over planes of cellular tissue which are so vulnerable. It would, of course, be better if we could avoid stomy altogether, but I still feel that this may be a valuable adjunct in the management of difficult problems; it may be most useful and effective as a secondary intervention in cases in which there is perhaps unusual difficulty in carrying out the repair or in which a secondary fistula exists.

**Ronald Belsey:** The transpleural route for the surgical correction of congenital atresia of the oesophagus offers the advantage of improved exposure for dissection of the upper and lower segments of the mediastinum when this is necessary to obtain approximation, and facilitates the end-to-end anastomosis. With intratracheal ether anaesthesia the lungs can be inflated at will and the dangers of a pneumothorax avoided. Pleural complications such as collection of fluid or infection must,

to see whether any passes through an upper fistula, and then withdrawn. Care is taken to see that none spills over into the lungs.

This method of examination confirms the diagnosis and also indicates the precise type of anomaly which is present (figs. 3 and 4).

#### THE OPERATION

Local anaesthetic. (Procaine 1%)

*Incision.*—Starting over the second right rib 1 cm. from the spine and curving downwards and outwards to end over the sixth rib. 2 cm. of the posterior portion of the fifth rib excised subperiosteally. The extrapleural plane is defined and the fourth, third and second ribs together with the intercostal bundle divided. The pleura is now gently displaced inwards until the vena azygos arch comes into view. If this is in the way it is divided between silk ligatures. Care must be taken in doing this. The upper segment is identified by moving the catheter in the blind sac. The lower end is found and ligated as close as possible to the trachea. Stay sutures are introduced and the lower segment divided and sutured to the upper segment. An opening is made in the upper segment and the anastomosis completed.

Help is obtained in completing the anastomosis by passing the nasopharyngeal tube down into the lower part of the œsophagus and so displaying the structures to be sutured.

The lower segment may be very delicate and attempts at making too complicated an anastomosis may result in the stitches cutting out.

A series of interrupted sutures, if possible using the "telescopic method" of Cameron Haight, in which the whole thickness of the lower segment is anastomosed to the mucous membrane of the upper segment, allowing the comparatively thick muscle of the upper segment to surround the anastomosis like a cuff, is probably the best.

Fine round-bodied eyeless needles carrying fine silk are suitable for the anastomosis and cleft palate instruments in general have been found satisfactory for the operation.

*After-care.*—Six hours after the operation penicillin solution is given by mouth and repeated hourly.

The child should be nursed in an oxygen tent and turned from one side to the other every hour to prevent pulmonary complications.

The hydration of the child is best left to an experienced pædiatrician.

In conclusion, I would urge that the possibility of œsophageal atresia be in the minds of all those who have the responsibility of caring for small infants in the first few hours of their life.

#### REFERENCES

- BRENNEMAN, J. (1918) *Amer. J. dis. Child.*, 16, 143.  
 FRANKLIN, R. H. (1947) *Lancet* (ii), 243.  
 — (1948) *Ann. Roy. Coll. Surg.*, 2, 69.  
 GAGE, M., and OCHSNER, A. (1936) *Ann. Surg.*, 103, 725.  
 GAMBLE, H. A. (1938) *Ann. Surg.*, 107, 701.  
 GIBSON, T. (1697) *The Anatomy of Humane Bodies Epitomized*, 5th Ed. London. P. 239.  
 GUTHRIE, K. J. (1945) *J. Path. Bact.*, 57, 367.  
 HAIGHT, C. (1944) *Trans. Amer. surg. Ass.*, 62, 623.  
 — (1944) *Ann. Surg.*, 120, 623.  
 — and TOWNSELY, H. A. (1943) *Surg. Gynec. Obstet.*, 76, 672.  
 HOLT, F. J., HAIGHT, C., and HODGES, F. J. (1946) *Radiology*, 47, 457.  
 HUMPHREYS, G. H. (1944) *Surgery*, 15, 801.  
 KEITH, A. (1910) *Brit. med. J.* (i), 301.  
 LADD, W. E. (1944) *New Eng. J. Med.*, 230, 625.  
 LANMAN, T. H. (1940) *Arch. Surg.*, 41, 1060.  
 LEVEN, N. L. (1939) *J. Thorac. Surg.*, 9, 213.  
 — (1941) *J. Thorac. Surg.*, 10, 648.  
 MACKENZIE, M. (1884) *Diseases of the Throat and Nose*. London.  
 O'REILLY, N., FRANKLIN, R. H., and DALEY, M. D. (1944) *Arch. Dis. Child.*, 19, 131.  
 PLASS, E. D. (1919) *Johns Hopk. Hosp. Rep.*, 18, 258.  
 RICHTER, H. M. (1913) *Surg. Gynec. Obstet.*, 17, 397.  
 SKELETON, A. C., and KNIGHT, M. D. (1944) *Ann. Surg.*, 119, 556.  
 R. G. GREY (1946) *Injuries and Diseases of the Œsophagus*. London.  
 E. C. (1929) *Amer. J. Roentgenol.*, 22, 463.

**Professor G. Grey Turner:** Only a few years ago it was thought that congenital atresia of the œsophagus was something beyond the scope of effective treatment of any sort. I can vividly remember the occasion which convinced me that we really must attempt something more for the relief of these doomed infants and that effective intervention would probably mean a direct attack at the site of the deformity itself, in fact exactly what has turned out to be the proper method of dealing with the anomaly. It was in Glasgow in December 1936: I had been lecturing on the œsophagus and was afterwards invited to inspect some pathological treasures which had been retrieved from the wonderful resources of the Children's Hospital in that City. I was expecting to find perhaps two or three rather good specimens of congenital anomalies of the œsophagus but instead a large bucketful of all types was produced for my examination. I was immensely impressed with the care that had been displayed by the late Brown Kelly in going into the pathological features of these conditions with the assistance of his friend, Professor Blacklock. It was that experience which made me realize that the condition must be much more frequent than had been supposed and that it was not just an interesting curiosity. Some œsophageal anomaly in the nature of atresia probably occurs in about 1:3,000 births but as most of the infants die of pneumonia the actual condition is not suspected nor is it disclosed at necropsy unless particularly looked for. After seeing this wealth of material at Glasgow I was convinced that we must devise a direct intervention at the site of the atresia and probably by the posterior mediastinal route (see Grey Turner, G., 1938, *Brit. med. J.* (ii), 1110). Such an exposure was tried out on a couple of stillborn infants and one also studied the problem in transverse sections of infant cadavers. These observations convinced me of the practicability of the proposed intervention while they emphasized the difficulties, due to the extreme smallness and delicacy of the parts concerned.

The opportunity to try the operation did not occur until the first case on which Mr. Franklin operated at my suggestion at the Postgraduate School in October of 1941. The delay was partly due to the fact that we had to depend on receiving our patients from the Maternity Department and partly because our efforts were distracted by other preoccupations in connexion with the late war. Incidentally, one or two experiences arising from bombing raids convinced me, of the remarkable recuperative capacity of infants of tender age and encouraged me to proceed with the major interference contemplated. It was about that time, when discussing the problem in the presence of our very welcome American visitors, that I learned for the first time that an American surgeon, Dr. C. Haight, had already operated with success in at least one case of atresia, though the case was not published until three years later (Haight, C., and Townsley, H. A. 1943, *Surg. Gynec. Obstet.*, 76, 672).

Delving further into the history has disclosed that very occasional attempts at direct intervention have been made since Richter was bold enough to make the suggestion as long ago as 1913. Even now I do not think a sufficient number of these cases come before the surgeon at the proper time and I believe that we still require to carry on propaganda among obstetricians, maternity nurses, midwives and even paediatricians directed to their early recognition. If surgical intervention is to be attended by a reasonable chance of success, it must be carried out before secondary pneumonic changes have taken place and that probably means within about forty-eight hours after birth. In connexion with the early diagnosis, I want to say a word about the avidity with which these little infants attempt to take food and with the striking cyanosis and accumulation of mucus which usually attends their efforts to swallow. So far as the actual operative interference is concerned, I would stress the wisdom of being ready prepared and of being furnished with suitable instruments and, for this purpose, I suggest that the instruments ordinarily used for cleft palate operations will probably be found to be most useful, especially long delicate forceps, fine needles and suitable reliable needle holders with long handles. Very fine tantalum wire may prove to be the best suture material. In suturing a tiny tube such as the infants' œsophagus I would utter a warning as to the need for very great care in not inadvertently making a stricture. Things should be so arranged that when the suturing is finished the lumen at the site is bigger than at other parts of the tube. To this end I should be inclined to advise that we should not attempt to use a single suture carried all round but that we should use either a series of interrupted sutures or an encircling stitch that is interrupted in such a way that only about a third of the tube is included in any one thread. Those who have had the most experience must lay down dicta for the guidance of the meeting but I should feel that it is probably a factor in the safety of the operation to provide a track to the surface from near the site of the anastomosis, so that if leakage does occur fluids can freely escape externally and will not be spread in the planes of cellular tissue which are so vulnerable. It would, of course, be better if we could avoid gastrostomy altogether, but I still feel that this may be a valuable adjunct in the management of these difficult problems; it may be most useful and effective as a secondary intervention in cases in which there is perhaps unusual difficulty in carrying out the repair or in which a secondary fistula develops.

**Mr. Ronald Belsey:** The transpleural route for the surgical correction of congenital atresia of the œsophagus offers the advantage of improved exposure for dissection of the upper and lower segments from the mediastinum when this is necessary to obtain approximation, and facilitates the end-to-end anastomosis. With intratracheal ether anaesthesia the lungs can be inflated at will and the dangers of an open pneumothorax avoided. Pleural complications such as collection of fluid or infection must,

however, be diagnosed and treated early. Early feeding by mouth, and the avoidance of tubes and enterostomies, should be aimed at.

Two important anatomical factors should be stressed. First, the blood supply to the upper centimetre of the lower segment may come from the wall of the trachea, and division of the tracheo-oesophageal fistula may lead to necrosis of this portion unless it is resected. The shortening of the lower segments will render the anastomosis more difficult but may lessen the risk of leakage at the suture line from ischaemic necrosis. Second, the blind upper segment may be densely adherent to the posterior wall of the trachea and division of those adhesions more than compensates for the shortening of the lower segment.

Baby O., aged 48 hours, was admitted to the Thoracic Unit at Frenchay on December 18, 1948, with suspected congenital atresia of the oesophagus. The diagnosis was confirmed by lipiodol instillation through a catheter into the blind upper segment. The X-ray showed collapse of the right upper lobe and the presence of much gas in the stomach and small bowel.

Under intratracheal G.O.E. anaesthesia the fifth right rib was resected postero-laterally, the lung retracted downwards, azygos vein doubly ligated and divided. The tracheo-oesophageal fistula was closed and an end-to-end one layer anastomosis between the oesophageal segments performed with stainless steel wire sutures. The lung was inflated and the chest closed without drainage. Convalescence was uneventful and the infant was allowed to feed normally forty-eight hours after operation. Barium swallow ten weeks after operation showed no stenosis and a normal oesophageal contour.

### Healed Miliary Tuberculosis of Liver and Spleen. Hepatomegaly, Splenomegaly.—

G. KONSTAM, F.R.C.P.

R. B., female, aged 12 years.

At the age of 18 months she developed Pott's disease of lumbar spine, psoas abscess and tuberculosis of the right ankle and was bed-ridden for two years. Then she made a good recovery and gained weight until one year ago when she began to get intermittent epigastric pain; in recent months her appetite has flagged and a week prior to admission to hospital on November 1, 1948, she became feverish and the abdominal pain returned.

*Family history.*—Mother has chronic pulmonary tuberculosis.

*On examination* (November 1948).—Remittent fever ranging between 97° and 102°. Well-nourished, dark-complexioned girl—not jaundiced. No enlarged glands felt. Heart and lungs normal. The liver was enlarged to three fingerbreadths below the costal margin, and was of firm consistency; the surface was irregular and protruded in the epigastrium where it was tender. The spleen was also enlarged down to the same level but was not tender.

There was a puckered scar from an old psoas abscess in the right groin.

Right ankle: limitation of dorsiflexion; right calf wasted.

*Investigations.*—Urine: No bile pigment, urobilinogen 3.32 mg. in twenty-four hours. Blood culture sterile. Serum agglutinations to T.A.B., *Br. abortus* negative.

*Blood-count.*—R.B.C. 4,340,000; Hb 92%; W.B.C. 12,400; Polys. 78%. Fragility normal. Van den Bergh 0.6 mg. (1.2 units). Blood W.R. negative. Plasma proteins, 2.11.48, total protein 9 grammes, albumin 5 grammes, globulin and fibrinogen 4 grammes. Alkaline phosphatase 49 units. Serum colloidal gold negative. Thymol turbidity 4.0 units. Takata-Ara reaction positive.

X-ray chest: no infiltration, calcified lymph nodes both hila. X-ray lumbar vertebrae: old Pott's disease L. 2 and 3, which are partly fused. L. 4 shows some deformity. Opacity to the right of these vertebrae suggesting calcification in psoas abscess. Calcification also present in region of liver.

*Course.*—The pyrexia continued and anorexia increased. In view of the enlarged and progressively tender liver a course of emetine 6 grains was given; although the temperature fell, her condition deteriorated and on December 4, penicillin 25,000 units (three hourly for nine days) was started. From then onwards she improved rapidly—the temperature and pulse settled and the liver tenderness disappeared.

Owing to the calcified X-ray opacity seen in the region of the liver, especially soft films were taken, and these revealed calcified miliary shadows scattered through the hepatic and splenic areas (fig. 1).

*Comment.*—The sequence of events in all probability was as follows: Aged 18 months, primary tuberculous focus in the lumbar vertebrae, followed by hæmatogenous spread and miliary lesions in the liver and spleen but not in the lungs (calcified foci only, in both hilar regions). The recent pyrexial illness with extreme hepatic tenderness may have been due to secondary pyogenic infection of a caseous focus in the liver, as response to penicillin was prompt.



FIG. 1.—Lateral X-ray of spine and liver showing old Pott's disease of L. 2, 3 and 4, with calcification in psoas. Note multiple calcified foci in liver.

Hoyle and Vaizey (1937) analysing 120 cases of chronic miliary tuberculosis collected from the literature found 13 with enlarged livers and 31 with big spleens, and only seldom were calcified miliary foci demonstrated radiologically. Miliary tuberculosis of the lungs, whether healed or not, was the rule and the absence of this is noteworthy in this case. These authors suggest, however, that chronic miliary lesions may occasionally heal leaving little or no permanent structural change.

Fibrosis around the miliary foci probably accounts for the enlargement of liver and spleen although the tough irregular surface of the liver in this case suggests a multilobular cirrhosis. Amyloidosis is unlikely in view of the return to good health and the absence of albuminuria. Braeuning and Redeker (1931) consider the prognosis relatively good when the miliary spread occurs in early childhood, soon after the primary infection.

#### REFERENCES

- BRAEUNING, H., and REDEKER, F. (1931) *TuberkBibl.*, 62, 160.  
 HOYLE, C., and VAIZEY, M. (1937) *Chronic Miliary Tuberculosis*. London.

[March 11, 1949]

**Four Cases of Intermittent Claudication.**—PETER MARTIN, M.Chir.

#### (1) Due to Thrombo-angiitis Obliterans

P. C., male, aged 37. March 1948 attended hospital complaining of intermittent claudication in the left leg with claudication distance of 200 yards.

June 1948: Popliteal neurectomy performed.

September 1948: Left lumbar sympathectomy.

Following popliteal neurectomy he has been able to walk any distance without pain and is back at work as a builder's labourer. The lumbar sympathectomy did not affect the claudication, but improved the circulation peripherally.

### (2) Due to Diffuse Obliterative Arteritis

R. S., male, aged 64. Retired barge-master. September 1947 attended hospital with severe intermittent claudication in the left leg.

Left popliteal neurectomy performed two weeks later. Relieved from pain and returned to work as skipper of a motor boat.

June 1948: Requested operation on right leg, and this performed.

January 1949: Severe claudication in left soleus with a claudication distance of 30 yards.

January 1949: Tenotomy of tendo Achillis left side.

Since then he has not returned to work but has been walking about comfortably for at least two miles with little disability resulting from the tenotomy.

### (3) Due to Diffuse Obliterative Arteritis

R. B., male, aged 55. Very severe claudication in the anterior tibial group of muscles in his right leg. Claudication distance of 20 yards when he was pulled up with intense pain.

January 30, 1949, external popliteal nerve crushed. Toe-spring fitted post-operatively. He is now getting about in comfort and can walk two miles without pain but has to go slowly.

### (4) Due to Diffuse Obliterative Arteritis

A. B., female, aged 61. Admitted to hospital July 1948 with bilateral claudication in the gastrocnemii. Left leg worse than right.

July 1948: Left popliteal neurectomy.

November 1948: She asked that the right leg should be operated on and this was done.

Now she can walk any distance, stand in queues and has to be dissuaded from running for buses.

*Comment.*—Sympathectomy in the treatment of intermittent claudication is unsatisfactory, uncertain and rarely successful and should not be undertaken with promise of relief. Boyd and Learmonth have suggested denervation of the gastrocnemius where this muscle is the origin of symptoms, which is often the case, and sometimes, particularly where the vascular obstruction is segmental as in thrombo-angitis obliterans, the results are gratifying and the disability resulting is minimal. I have employed this procedure with success following arterial embolism. If the obliterative disease of the arteries is diffuse and progressive, popliteal neurectomy is disappointing as the remaining calf muscles may soon begin to cause symptoms. In such cases it is preferable to defunction the whole group by tenotomy of the tendo Achillis, particularly if the patient's activity is severely limited by pain. Surprisingly enough, the disability again is not very severe and in these subjects physical endeavour has generally given place to slipped ease or a visit to a friend, to church or to the local public house and ability to accomplish this without pain is a source of relief and gratification. Claudication in the anterior tibial group may be very severe and may result in extreme disability. This group may be defunctioned by division or crushing of the external popliteal nerve and a toe-spring can be fitted to counteract the resulting foot drop. In the foot I have relieved pain by injection of a few cubic centimetres of proctocaine into the tender claudicating muscle but have not as yet tried the effect of a neurectomy of the plantar nerves.

The cases described are illustrative of some of these procedures and I can testify that in spite of occasional resulting disability the patients are grateful.

It is, of course, important not to treat cases which show an incipient gangrene, or marked skin or colour changes and I restrict choice of patients to those with healthy skin and subcutaneous tissues. An ill-advised defunctioning may lead the patient to an activity which will precipitate gangrene.



**Intermittent Claudication and Abdominal Aneurysm.**—E. IDRIS JONES, M.D.

Male, aged 57. Had angina of effort, summer 1948. For last six months has had pain in one calf on exercise, restricting walking to 25 yards. Pain passes off on rest.

In January 1949 pulsation absent in all vessels of left leg, present in right leg. Large abdominal aneurysm, 4 inches in diameter to left of mid-line. B.P. 170/90 in right arm and 134/54 in right leg. Heart: Aortic systolic murmur present. No other abnormal physical signs.

*Investigations.*—W.R. and Kahn negative. E.C.G.: Left axis deviation. X-ray chest: Left ventricle enlarged.

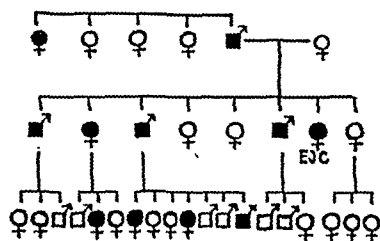
On 11.3.49 the aneurysm was much smaller, now about 2 inches in diameter and probably arising from left common iliac artery. Pulsation still absent in vessels of left leg. Exercise tolerance now 100 yards.

**Familial Haemorrhagic Telangiectasia (Rendu-Osler-Weber Disease).**—W. A. BOURNE, M.D., and J. K. WAGSTAFF, M.R.C.P.

Miss E. J. C., aged 76. Haemorrhage from age 24, usually epistaxis, but initiated by bleeding from lip. At the age of 50 she had hæmoptysis. At 68 she had severe bleeding from tongue. Admitted to hospital in Brighton: extensive diathermy. At the age of 74, the severity increased. Dyspnœa and dependent œdema developed. There is no hæmaturia or gastro-intestinal hæmorrhage. Katamenia ceased at age 50: no evident relation to hæmorrhage. No Raynaud's syndrome.

*Family history.*—Patient states she is only member of family presenting telangiectases, epistaxis being a recognized manifestation. Two sisters died of pulmonary tuberculosis.

*Present admission.*—Yellowish, œdematous. No koilonychia. Telangiectases of tongue, lips, face, pulps of fingers and thumbs, and under one nail. Heart enlarged to left with systolic apical bruit. B.P. 160/80. Lungs normal clinically. Liver and spleen not enlarged. Blood: R.B.C. 2,740,000; Hb 34%; C.I. 0.63; W.B.C. 7,200, normal differential. Elliptocytosis not found. Platelets, and bleeding, clotting and prothrombin times normal. Clot retraction poor. Liver function normal.



Familial haemorrhagic telangiectasia.  
Pedigree of Miss E. J. C. The sex sign  
is shown in black in affected persons.

*X-ray examination.*—Chest: Calcified glands in hilar regions; abdomen: no splenic enlargement, but atheromatous calcification of aorta, splenic artery and branches demonstrated; pelvis: Paget's disease of left innominate bone.

*Treatment.*—Blood transfusion. Iron. Topical thrombin. Oxycel gauze. Rutin, 500 mg. daily in divided doses.

*Comment.*—This case, originally seen by Dr. Sequeira in 1897, is believed reported, with pedigree, for the first time. Hæmoptysis is doubtfully attributable to the vascular lesion in view of the strong tuberculous history. Rarer complications are not present. Rutin is not thought to have helped in this, nor in another case in which it was tried.

**Non-familial Hemorrhagic Telangiectasia.**—W. A. BOURNE, M.D., and E. L. WATSON, M.D., I.P.

Mrs. E. L., aged 32, has had pain in legs and feet since birth. At about eight months of age the first (small) capillary nevus appeared over right shin. Since normal termination of her pregnancy, nevus has become red and has pained one or two days before appearance of period, and within two of their approach. Remains so during first two days of period, which have duration nine days. Frequency twenty-eight days, less previous than at onset.

Six months ago she developed nose-bleeding during first two days of every period. No change in course of it and time of primary condition of small spider telangiectasia on hand.

**Facial changes.**—Tumidities and nasal bleeding. Acute priapism and parasthesia upper and lower extremities.

**Family history.**—Negative for hemorrhage and telangiectasia. One sister has threatened abortion.

**On examination.**—Capillary nevus over right shin is certainly more prominent during menstruation, becoming much darker at onset. Perioral tumidity of lower and upper lip prominent and a few spider nevi on hands and feet are not so affected. No local skin change found elsewhere.

**Comments.**—Observation of case has not confirmed relation of red palms and spider nevi to hereditary type of hemorrhagic disease. They may indicate local capillary dysplasia. Relation of nevus on leg and sprains to menstruation is, however, definite. Spider telangiectasia in response to sex hormones in pregnancy and liver disease possibly involves a different mechanism—telangiectasia and overgrowth of Kohn's sinuses arising from capillary change such as appears in this case in the leg and nose.

The two cases demonstrate telangiectasia and sprains arising from different causes—hereditary defect and abnormal uterine.

Dr. E. P. Davis Dr. Bourne's first case is a new example of hereditary hemorrhagic telangiectasia. The character is suggested by symptoms as a telangiectasia syndrome, but additions to the case are valuable. As regards treatment, I have been disappointed in the efficacy of radium and am wondering if it has any real value.

## Section of Comparative Medicine

President—Professor WILSON SMITH, M.D., F.R.S.

[February 16, 1949]

### DISCUSSION: THE SIGNIFICANCE OF STRAIN DIFFERENCES IN VIRUS PROPHYLAXIS. [Abridged]

Dr. W. M. Henderson, *Research Institute (Foot-and-Mouth Disease Research Committee), Pirbright, Surrey*: There must be few virus diseases in which "strain differences" are not of importance in prophylaxis. I shall deal, mainly, with the significance of strain differences in one disease of animals, namely, foot-and-mouth disease. I believe it is true to say that in this disease the significance of strain differences is so great that their occurrence is one of the biggest obstacles in the way of control by immunization.

It is noteworthy that foot-and-mouth disease was the first disease of animals or man in which the filtrable nature of the virus was demonstrated. It was also the first virus disease in which the occurrence of major immunological differences was discovered. Vallée and Carré in 1922 [1] reported the existence of two quite distinct immunological types, Vallée O and Vallée A. In 1926, Waldmann and Trautwein [2] described the isolation of strains of a third type, Waldmann C. Strains of virus isolated from the great majority of outbreaks of foot-and-mouth disease can be classified as belonging to one of these three immunological types. Infection with one type, although conferring immunity to strains of the homologous type, leaves the animal susceptible to infection with strains of other types. The existence of this extreme strain difference is of such obvious importance in prophylaxis that for the purposes of this discussion it requires but brief mention. This characteristic of foot-and-mouth disease virus is not peculiar amongst the viruses causing disease in animals. Similar gross immunological differences between strains are found in vesicular stomatitis of horses, cattle and swine (at least two types); vesicular exanthema of swine (four types have been recorded); equine encephalomyelitis (at least three types) and in African horse sickness (from the published evidence it is difficult to appreciate whether the magnitude of the antigenic differences between strains is as great as in those diseases just cited). This is in contrast to the position among the virus diseases of man as, so far, the natural occurrence of major strain differences has been demonstrated in only one disease, namely, influenza.

Besides the existence of these immunological types, in foot-and-mouth disease at least, there are a number of other strain differences that must be considered.

The first is a difference in immunogenicity as judged by the potency of vaccines when tested against the strain of virus from which they were prepared. For example, comparing the protection established in cattle by inactivated virus vaccines prepared from different strains we find the 50 per cent protection dose against homologous virus infection may be as small as 9 c.c. for one strain and as large as 70 c.c. for another strain.

We have no information whether this difference is an actual difference in the immunogenicity of the strain or whether it is a difference in the sensitivity of the strains to the treatment given during the preparation of the vaccine. When we are studying vaccines which involve in their preparation the use of some physical or chemical agent to "inactivate" the virus it is not possible to say whether the amount of antigen available for immunizing purposes is always the same even although the precaution has been taken of estimating by titration the amount of active virus present in the starting material. It must be pointed out that it has still to be shown that the immunogenic differences demonstrated when using one inactivating agent are going to be equally apparent when using another. There is no doubt, however, of the existence of this difference between the protective capacity of vaccines of the same method of preparation, prepared from different strains. In our experience it means that this quality of a newly isolated strain must be examined before it can be assumed that the strain is suitable for use in vaccine production.

Another strain difference that is of considerable practical importance, if one is dependent on the infected animal as the source of virus for vaccine production, is reflected in variation in the yield of infective material, or in the virus content of the infective tissues or fluids. This factor is, of course, greatly affected by the susceptibility of the host but considerable differences in virus content can be demonstrated from observations on many cattle of the same source, age and breed.

To come to the most interesting strain difference of all, the differences in antigenic behaviour found between strains of the same immunological type. The possibility of the existence of such differences in antigenic behaviour was, without doubt, suspected from time to time but it was not until large scale attempts were made to control the disease by vaccination that much attention was given to their occurrence. More recently, the development of the complement-fixation test for type determination has greatly increased the

**Non-familial Hæmorrhagic Telangiectasia.**—W. A. BOURNE, M.D., and J. K. WAGSTAFF, M.R.C.P.

Mrs. E. K., aged 32. Had red palms as long as she can remember. At about third month of second (latest) pregnancy capillary nævus appeared over right tibia. Since normal termination of this pregnancy, nævus has become red, hot and painful one or two days before appearance of periods, and warns her of their approach. Remains so during first two days of periods, which have duration nine days, frequency twenty-eight days, loss profuse, pain at onset.

Six months ago she developed nose-bleeding during first two days of every period. No change she is aware of at that time in palmar condition or small spider telangiectases on hands.

*Past history.*—Tonsillitis and breast abscess. Recent pains and paræsthesiæ upper and lower extremities.

*Family history.*—Negative for hæmorrhage and telangiectasia. One sister has rheumatoid arthritis.

*On examination.*—Capillary nævus over right shin is certainly more prominent during katamenia, becoming much fainter in intervals. Nævroid redness of thenar and hypothenar eminences and a few spider nævi on hands and face are not so affected. No local cause found for epistaxis.

*Comment.*—Observation of case has not confirmed relation of red palms and spider nævi to menstrual cycle or rheumatoid disease. They may indicate local capillary dysplasia. Relation of nævus on leg and epistaxis to menstruation is, however, definite. Spider telangiectasia as response to sex hormones in pregnancy and liver disease possibly involves a different mechanism (enlargement and overgrowth of Renaut's nutrient arteries) from capillary change such as appears in this case in the leg and nose.

The two cases demonstrate telangiectasia and epistaxis arising from different causes—anatomical defect and hormonal stimulus.

**Dr. C. P. Petch:** Dr. Bourne's first case is a clear example of hereditary hæmorrhagic telangiectasia. The character is regarded by geneticists as a Mendelian dominant, but additions to the data are valuable. As regards treatment, I have been disappointed in the efficacy of rutin, and am wondering if it has any real value.

## Section of Comparative Medicine

President—Professor WILSON SMITH, M.D., F.R.S.

[February 16, 1949]

### DISCUSSION: THE SIGNIFICANCE OF STRAIN DIFFERENCES IN VIRUS PROPHYLAXIS. [Abridged]

Dr. W. M. Henderson, *Research Institute (Foot-and-Mouth Disease Research Committee), Pirbright, Surrey*: There must be few virus diseases in which "strain differences" are not of importance in prophylaxis. I shall deal, mainly, with the significance of strain differences in one disease of animals, namely, foot-and-mouth disease. I believe it is true to say that in this disease the significance of strain differences is so great that their occurrence is one of the biggest obstacles in the way of control by immunization.

It is noteworthy that foot-and-mouth disease was the first disease of animals or man in which the filtrable nature of the virus was demonstrated. It was also the first virus disease in which the occurrence of major immunological differences was discovered. Vallée and Carré in 1922 [1] reported the existence of two quite distinct immunological types, Vallée O and Vallée A. In 1926, Waldmann and Trautwein [2] described the isolation of strains of a third type, Waldmann C. Strains of virus isolated from the great majority of outbreaks of foot-and-mouth disease can be classified as belonging to one of these three immunological types. Infection with one type, although conferring immunity to strains of the homologous type, leaves the animal susceptible to infection with strains of other types. The existence of this extreme strain difference is of such obvious importance in prophylaxis that for the purposes of this discussion it requires but brief mention. This characteristic of foot-and-mouth disease virus is not peculiar amongst the viruses causing disease in animals. Similar gross immunological differences between strains are found in vesicular stomatitis of horses, cattle and swine (at least two types); vesicular exanthema of swine (four types have been recorded); equine encephalomyelitis (at least three types) and in African horse sickness (from the published evidence it is difficult to appreciate whether the magnitude of the antigenic differences between strains is as great as in those diseases just cited). This is in contrast to the position among the virus diseases of man as, so far, the natural occurrence of major strain differences has been demonstrated in only one disease, namely, influenza.

Besides the existence of these immunological types, in foot-and-mouth disease at least, there are a number of other strain differences that must be considered.

The first is a difference in immunogenicity as judged by the potency of vaccines when tested against the strain of virus from which they were prepared. For example, comparing the protection established in cattle by inactivated virus vaccines prepared from different strains we find the 50 per cent protection dose against homologous virus infection may be as small as 9 c.c. for one strain and as large as 70 c.c. for another strain.

We have no information whether this difference is an actual difference in the immunogenicity of the strain or whether it is a difference in the sensitivity of the strains to the treatment given during the preparation of the vaccine. When we are studying vaccines which involve in their preparation the use of some physical or chemical agent to "inactivate" the virus it is not possible to say whether the amount of antigen available for immunizing purposes is always the same even although the precaution has been taken of estimating by titration the amount of active virus present in the starting material. It must be pointed out that it has still to be shown that the immunogenic differences demonstrated when using one inactivating agent are going to be equally apparent when using another. There is no doubt, however, of the existence of this difference between the protective capacity of vaccines of the same method of preparation, prepared from different strains. In our experience it means that this quality of a newly isolated strain must be examined before it can be assumed that the strain is suitable for use in vaccine production.

Another strain difference that is of considerable practical importance, if one is dependent on the infected animal as the source of virus for vaccine production, is reflected in variation in the yield of infective material, or in the virus content of the infective tissues or fluids. This factor is, of course, greatly affected by the susceptibility of the host but considerable differences in virus content can be demonstrated from observations on many cattle of the same source, age and breed.

To come to the most interesting strain difference of all, the differences in antigenic behaviour found between strains of the same immunological type. The possibility of the existence of such differences in antigenic behaviour was, without doubt, suspected from time to time but it was not until large scale attempts were made to control the disease by vaccination that much attention was given to their occurrence. More recently, the development of the complement-fixation test for type determination has greatly increased the

facility with which possible "variant" strains can be detected. Much work remains to be done, however, before the true significance of differences in degree of fixation of complement can be appreciated, especially when it comes to the correlation between the results of *in vitro* tests, serum-neutralization tests and vaccination experiments.

Traub and Möhlmann [3], in Germany, attempted to determine the significance as regards vaccination of complement-fixation differences between three A-type variants. Unfortunately their protocols are not available but they state that although each vaccine gave some protection against all three strains, greater protection was seen against the homologous strain than against the heterologous strains.

At Pirbright, the results of studies of strains of virus recovered from outbreaks in Mexico have provided us with the most comprehensive information we have on differences in antigenic behaviour between strains of the same type. This work, some of which I shall now describe, was done along with my colleagues, Dr. Ian A. Galloway and Dr. J. B. Brooksby [4, 5, 6, 7].

Having classified the strains isolated from Mexico as belonging to Vallée A type, the most important questions were whether vaccine prepared from a stock A type strain of high immunogenicity would protect cattle against infection with Mexican strains of virus and what was the level of immunogenicity of the Mexican strains when used for vaccine production.

A vaccine prepared from our best A type immunizing strain (strain 119) did not, when administered in equivalent dose, give the same measure of protection against infection with Mexican strain MP as it did against infection with strain 119. Six of eight cattle that had received a 30 c.c. dose of vaccine were completely protected against strain 119 infection, whereas all of another group of eight vaccinated cattle reacted on exposure to strain MP infection.

Cross serum-neutralization tests and complement-fixation tests with these two strains showed greater homologous neutralization and fixation respectively. Similar tests were then carried out with Mexican strain MP and a more recently isolated Mexican strain, strain M1. Here again greater homologous neutralization and fixation were observed in relation to one another and also to strain 119. In view of this difference between strains MP and M1 as shown by these results, their behaviour in a vaccination experiment was investigated. Although vaccine prepared from each strain gave better protection against the homologous virus infection, the differences in the results between the two groups were not sufficiently great to show more than a trend towards slight antigenic dissimilarity.

The question naturally arose of whether a large dose of vaccine would mask the type of antigenic dissimilarity found between strain 119 and the Mexican strains. It has been seen how a 30 c.c. dose of a strain 119 vaccine gave no protection against strain MP infection. In this next experiment groups of eight cattle, vaccinated with 100 c.c. doses of a strain 119 vaccine, were tested against strains 119, MP, and M1 by tongue inoculation. In the group tested with strain 119 six animals showed no reaction and two had primary lesions only. All of each group tested with strain MP and strain M1 respectively developed primary lesions and, in each case, five of the eight developed secondary lesions. All the cattle in the unvaccinated control groups showed complete development of primary and secondary lesions. Thus, even with a large dose of vaccine, the dissimilarity was still apparent.

The practical importance of all this was that the outcome would be uncertain of attempts to control the epizootic in Mexico by the use of stock A type vaccines supplied by different Institutes until information became available on the range of antigenicity of the A type strains used in their preparation. Furthermore, vaccines prepared from Mexican strains should include strains MP and M1 and the isolation and examination of strains should continue for the duration of the epizootic so that further differences in antigenic behaviour might be detected and taken into account.

It is not possible to give any idea of the frequency of occurrence of this type of difference but an apparently close relationship has been found between other strains widely separated as regards origin and time of isolation.

It can be seen how, with a veterinary problem such as this, it is possible to perform vaccination experiments under controlled conditions using the natural host of the infection. It is further possible to perform serum-neutralization experiments using virus and serum collected from the natural host, and to use this host as the "laboratory" animal for detection of virus. Change in this kind of procedure need only be made in the complement-fixation test when strains of virus must be adapted to the guinea-pig for the preparation of antisera. It is of great comparative interest, therefore, to see what evidence can be presented from the results of these tests on the correlation between the *in vitro* methods and the attempt at prophylaxis. One way of summarizing this evidence is shown in diagrammatic form in fig. 1. It will be seen throughout that there is greater homologous fixation of complement, greater homologous neutralization of virus and greater protection against the homologous virus infection and that each type of test places the virus strains in the same order in relation to each serum or vaccine.



Here, according to Sabin and Schlesinger [3] there are more probably at least three serological types, only one of which has been adapted to infect mice. The three types have probably, as have subtypes of influenza A, an antigen in common.

The serological types of arthropod-borne encephalitis viruses are so distinct and so stable that the viruses are called by different names. Thus, we have the forms of encephalitis known as St. Louis, eastern, western and Venezuelan equine, Japanese B and a few others. There are cross-reactions within this group, both with the complement-fixation and neutralization tests [4], so it is fair to bring them into a discussion of strain differences. Vaccine-prophylaxis has been shown to be possible within this group, but is in the experimental stage as regards man.

The viruses of the psittacosis family offer a different sort of problem. Here there exist a number of related viruses, having biological differences, but so closely similar antigenically that they can only be differentiated by the use of special techniques: there are psittacosis from parrots, ornithosis (a related set of viruses from other birds), mouse pneumonitis, cat pneumonitis, lymphogranuloma venereum, and several strains of pneumonitis viruses from human sources. These differences do not concern us from the point of view of prophylaxis, and we may thankfully turn away from a nasty knotty problem.

#### INFLUENZA

*Antigenic variation in influenza viruses.*—All human influenza viruses yet known fall into one of two groups, A or B, antigenically unrelated, or almost so. Swine influenza is related to A. Within the A group (and within the B group) are minor differences between strains. Though "minor" they are sufficiently large to affect the results of attempts at vaccine-prophylaxis. Differences were first recognized by means of cross-neutralization and cross-immunity tests in mice. It was found that almost any strain was better neutralized by homologous than by heterologous immune sera. In 1936-37 Smith and Andrewes [5] found four strains (W.S., Gatenby, Christie and Talmey) which seemed more specific than others, and strains turning up in later years were compared against these four specific strains. Most of those occurring between 1937 and 1946 were found to be more closely related to Christie and Talmey than to others. They were related also, with varying degrees of closeness, to the classical American and Australian strains, PR8 and Melbourne. It was, however, possible to obtain widely different ideas as to relationships, if different methods of comparison were used. Besides cross-neutralization and cross-immunity tests in mice, one can employ cross-immunity tests in ferrets, hemagglutination, neutralization tests in eggs and complement fixation with two kinds of antigens. Complement fixation with non-specific soluble antigens differentiates between viruses A and B with certainty, but takes no account of lesser strain differences. The other tests are apt to give results very hard to interpret, as Glover and I [6] found when trying to discover the relationships of British swine influenza viruses to other strains. No two tests gave quite the same answers.

This, then, was the position. Whenever a new strain of virus was isolated, it was found to be rather different from classical strains such as PR8; but we had no knowledge of relationships amongst viruses recovered in different countries in one year, or in one country in successive years. A vaccine trial in the U.S.A. in 1943 gave very promising results, possibly because the vaccine used had, incorporated in it, a recently isolated (Weiss) strain [7]. Then in 1947 vaccines used both here [8] and in America quite failed to give any protection. The A viruses isolated were decidedly remote antigenically from those used to make the vaccine, and there is little doubt that this fact explains the failure of the vaccines. Where were we to go from here? An unofficial group considering the matter at the 1947 International Microbiological Congress in Copenhagen felt that study of virus strains on an international basis was called for. As a consequence of its recommendations, the World Health Organization asked the Medical Research Council to set up in London a World Influenza Centre to promote co-operation in this field. Its objects were to collect information and, more particularly, strains of virus from epidemics anywhere in the world. It was thus hoped to learn how far apparently new strains of virus caused outbreaks by travelling from country to country, and to attempt classification of influenza viruses on an orderly basis. This centre is now in being at the National Institute for Medical Research, and has been having its first practical trial during the recent Continental influenza epidemic. Viruses have been received from Italy, Switzerland, France and Holland, as well as from this country. These have been studied antigenically and, without waiting for full antigenic study, distributed in the dried state to laboratories in eight different countries. What we have learnt has made me begin to change my ideas on the epidemiology of influenza. I confess that I had the idea that influenza A was almost infinitely labile, that as fast as we made a vaccine the virus would produce another antigenic variant and so always keep one jump ahead of us. The only hope of effective vaccination might then be to obtain virus (as we have just done) from one country, and send it away rapidly to laboratories abroad, so that homologous vaccine might be made there in time to defend the inhabitants against prospective invasion. In fact, it is very doubtful if there would ever be time to do this effectively.



But now I am more hopeful. Strains recovered from this epidemic across the channel seem to be closely related to the strains which occurred in 1947. This antigenic type of virus first appeared in Australia in May 1946, though a 1944 Swedish strain may be related; at the beginning of 1947 it caused outbreaks in Britain, Holland and Sweden and in the U.S.A. In America they call this type A-prime, as it seems to stand rather apart from other A viruses. I do not myself like the term A-prime; it has unspecified limits and is an awkward term for those of us who are at the beginning of attempted classification of the group; one cannot see how it will fit tidily into a final orderly arrangement. These strains, which I shall refer to for convenience as 1947 A, seemed at that time rather homogeneous.

Now, the widespread occurrence of a new type of A seems to me to be surpassed in interest only by the virtual disappearance as an important cause of disease of the older A viruses related to PR8. Unless they stage a comeback, we may have to record that, at any rate in Britain and America, they had their swan song in the autumn of 1943. The original strain of A, W.S., recovered in 1933 and perhaps 1934, has never been recognized since in the wild state. Were we at that time at the tail of a dominance of W.S. virus? Have we just been through a decade in which PR8-like viruses were dominant, and have we but lately entered on an era in which prevalent A viruses are related to the 1947 strains? If so, we may be more hopeful of being able to make a vaccine of the topical strain and to use it effectively for a period of years. We shall, on this hypothesis, expect our vaccines to fail us every decade or so, until we have the measure of some new strain. Also, we can always hope that the mutability of influenza A is not infinite and that we may one day have the main possible variants neatly docketed. One can conceive that in the future a polyvalent vaccine may be available; or, alternatively, that the World Influenza Centre will be able to advise countries as to what is coming to them, so that the appropriate vaccine may be taken out of the cold stores where it is all ready and distributed rapidly wherever needed.

I will admit that, in talking thus, I am running a little ahead of my facts. We still lack a satisfactory way of estimating how closely A viruses are related to each other. Though we may strongly suspect it, it is not really certain that all the strains of the 1936-46 decade were more closely related to each other than to the earlier, W.S., or to the later, 1947, strains. In fact, I plead guilty to an attempt at over-simplification. I feel, however, that one is occasionally justified in making a heroic effort to see the wood in spite of the trees. In America, a strain study centre under Dr. Magill has been for some time engaged in trying to unravel the interrelations of strains. My colleagues, Drs. Fulton and Dumbell [9], have lately been attempting the feat by the use of a modified complement-fixation test, involving the specific, not the unspecific, "soluble" antigen. I feel that if this obscure problem could only be clarified the epidemiology of the disease would be much easier to understand. There is one final complication: Several workers, particularly Hirst [10], have adduced evidence of antigenic changes in strains in the laboratory, consequent upon passage through mice or other experimental animals. The occurrence of such changes seems established; probably, however, they are of minor importance compared with the gross differences between strains such as have significance for epidemiology and prophylaxis. It must be remembered also that animals injected with complex antigens may produce sera of which the antibody populations are not identical, since the animals may show different quantitative responses to the various ingredients injected. Small differences may thus be exaggerated. A remedy is to use pools of sera from several individuals; over-nice distinctions will be thus less likely to intrude themselves.

*Influenza B:* This virus seems to be less important as a cause of widespread epidemics than A; it seems more apt to exist in an endemic form. Moreover, it seems to be a better antigen than A, so that immunity to one variant may be effective against other variants within the B group. In any case, its vagaries have been less studied than for virus A.

Though it bears rather indirectly on prophylaxis, I may perhaps be allowed to suggest a line of enquiry which most intimately concerns comparative pathology. This arises from my tentative suggestion that a broad antigenic group of virus A may become dominant as a cause of human influenza over a period of years. We still do not know where human influenza virus goes to between epidemics. Shope [11] has shown how in the American Middle West swine influenza can be carried on, within lung-worms, from one season to another. The same has not, however, been shown as yet for Britain and other parts of the world. It is not inconceivable that the pig may act as a reservoir for human influenza. British strains of swine influenza are antigenically distinct from Shope's Iowa strain, but not clearly to be separated from human A viruses in general [6]. It would seem worth comparing serologically swine influenza strains with human ones occurring in the same year and country. If, for example, one were at this time to find swine influenza strains having some relationship to 1949 A, the hunt would be definitely up. So, too, it would be important to know whether viruses from odd cases of sporadic influenza in a no-flu year were serologically close to the strains from preceding or following epidemics; such a finding would suggest that man himself was after all the only reservoir to be considered.

The problems of foot-and-mouth disease surely touch on those of influenza—and probably of poliomyelitis and many other virus infections.

#### REFERENCES

- 1 HORGAN, E. S., HASEEB, M. A., and SATTI, M. H. (1948) *Brit. J. exp. Path.*, 29, 347.
- 2 FLORMAN, A. L., and TRADER, F. W. (1947) *J. Immunol.*, 55, 263.
- 3 SABIN, A. B., and SCHLESINGER, R. W. (1945) *Science*, 101, 640.
- 4 HAVENS, W. P., WATSON, D. W., GREEN, R. H., LAVIN, G. I., and SMADEL, J. E. (1943) *J. exp. Med.*, 77, 139.
- 5 SMITH, W. S., and ANDREWES, C. H. (1938) *Brit. J. exp. Path.*, 19, 293.
- 6 GLOVER, R. E., and ANDREWES, C. H. (1943) *J. comp. Path.*, 53, 329.
- 7 SALK, J. E., MENKE, W. J., Jr., and FRANCIS, T., Jr. (1945) *Amer. J. Hyg.*, 42, 57.
- 8 MELLANBY, H., DUDGEON, J. A., ANDREWES, C. H., and MACKAY, D. G. (1948) *Lancet* (i), 978.
- 9 FULTON, F., and DUMBELL, K. R. (1949) *J. gen. Microbiol.*, 3, 97.
- 10 HIRST, G. K. (1947) *J. exp. Med.*, 86, 367.
- 11 SHOPE, R. E. (1941) *J. exp. Med.*, 74, 49.

[March 16, 1949]

### DISCUSSION: THE PHARMACOLOGICAL BASIS OF MODERN ANÆSTHESIA

**Dr. Andrew Wilson:** The use of the terms "general" and "local" anæsthetic has recently undergone some modification and it is now more usual to reserve the term anæsthetic to describe those agents which produce generalized loss of sensation with loss of consciousness.

The pharmacology of modern anæsthesia also includes those drugs whose actions are designed either to prevent the side-effects of the anæsthetic substance, or to diminish the amount of anæsthetic required. So there are perhaps two major aspects for discussion: (1) The anæsthetic itself and the measures adopted to make the anæsthetic safe for the patient. (2) The premedication drugs which are designed to make the patient safe for the anæsthetic. I propose to confine myself to a consideration of the first aspect.

The anæsthetic agents are mostly simple aliphatic compounds which cause a reversible depression of living tissue. When used in moderate concentrations, these substances produce essentially a descending paralysis of the central nervous system which begins in the cortex, progresses to the spinal cord and finally affects the vital centres in the medulla. This is the basis of the different degrees of anæsthesia described by the anæsthetist.

For an explanation of the action of anæsthetics on the central nervous system, three essential factors must be taken into account: (1) The nature of the drug. (2) The high sensitivity of the brain cells for the drug. (3) The fact that the blood flow in the brain is greater than in most other tissues.

Many of the theories which have been advanced to explain the phenomenon of narcosis or anæsthesia, however, are based on the study of only one of these factors.

*Mode of action.*—The drugs which are used as anæsthetic agents differ greatly in structure, for they include hydrocarbons, alcohols, ethers, urethanes, sulphones and amides. It has therefore not been possible, except in the case of homologous series, to show any relationship between action and chemical constitution. For this reason, perhaps, many of the theories of narcosis have been founded on an exploration of certain physical properties of the drugs. Thus a correlation has been established between anæsthetic action and the relative solubilities of certain substances in the lipid and non-lipid constituents of the cell. This aspect of the subject was studied nearly a hundred years ago by Von Bibra and Harless and was later extended by the work of Meyer and Overton, who showed that there is a relationship between anæsthetic activity and the distribution coefficient of certain drugs in a lipid/water system.

Various other phenomena have been described such as changes in viscosity and the loss of water or dehydration produced in the cells; and with increased technical facilities it has been shown that there is an alteration in the permeability of the plasma membrane of the cells. These observations, however, fail to give more than an indication of how the drug may gain access to the cells or cell surfaces. They do not afford any explanation of how the drugs influence the function of the cell. For it must be remembered that one of the essential features of anæsthetic activity is its reversibility.

The functions of the cerebral cortex are readily depressed by altering its blood supply and there is well-substantiated evidence of the relationship between the physiological activity of the brain and its utilization of oxygen and of glucose. There is little doubt that this relationship is influenced by anæsthetics. Thus Lázló and his colleagues [1] have shown that during ether anæsthesia, the arterial venous oxygen difference falls from 3.7 to 2.2 vols. %, a decrease of 40%. Again, when the cerebral circulation of the dog is perfused at a constant rate with pentobarbitone [2], the oxygen uptake of the brain and utilization of sugar is reduced by 30%.

Considerable light has been thrown on the subject by the work of Quastel and his colleagues [3, 4] on the effect of the anæsthetics on the uptake of oxygen by brain tissue. In a series of well-designed experiments they have demonstrated, in a variety of animals, that

the respiration of brain tissue is inhibited by drugs such as ether, chlorotone, and barbiturates, in concentrations which cause deep narcosis. Furthermore, they have shown that this effect is rapid and reversible and that the sensitivity of the brain tissue is in marked contrast to that of the kidney, liver, spleen and testis.

The oxidation by the brain of glucose, sodium lactate and sodium pyruvate is inhibited much more readily than is that of glutamic acid. The fact that under these conditions the oxidation of succinate and p-phenylene diamine is not affected suggests that anaesthetics exert their inhibitory effects at two possible stages. Either (1) by interfering with the transfer of hydrogen from reduced cozymase to flavoprotein, or (2) by preventing the oxidation of flavoprotein by the cytochrome system by means of electron transfer (see fig. 1).

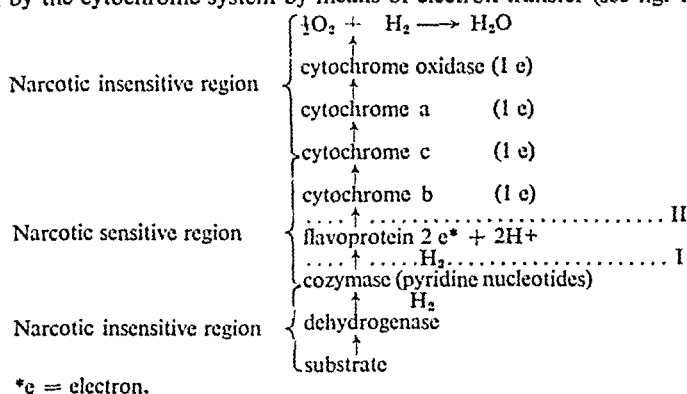


FIG. 1.—After Greig [5].

Now Greig [5] has indicated that since nembutal does not cause accumulation of reduced cozymase, the interference is not at position 1. Further proof that the inhibition probably occurs at position 2 is provided by a very neat series of experiments which Greig [6] has recently reported. It is known that in guinea-pigs deprived of vitamin C, the action of nembutal is prolonged and that this effect is considerably reduced when the animals are given ascorbic acid. Greig has shown that the addition of ascorbic acid to brain suspensions in the presence of nembutal diminishes the inhibition of glucose metabolism of brain produced by nembutal. She has suggested that the function of ascorbic acid in these circumstances is to offer an alternative route for the oxidation of carbohydrate, by providing a by-pass between the flavoprotein stage and cytochrome C.

In the case of the volatile anaesthetics, ether and chloroform, the acetylcholine metabolism of the central nervous system is more directly affected than by the barbiturates. Feldberg and others have suggested that this may account for the excitatory effects of the induction stage of  $CHCl_3$  or ether anaesthesia. It is known that the different areas of the brain differ greatly in their ability to synthesize acetylcholine and also in their content of cholinesterase. It is therefore not unreasonable to suggest that the different effects of the volatile anaesthetics and the barbiturate drugs may depend largely upon their different sites of action. There is, however, one point in common. Since the synthesis of acetylcholine is dependent on carbohydrate metabolism it is also possible that the different drugs affect this synthesis of acetylcholine at different stages.

The validity of much of this evidence is limited by the fact that all these *in vitro* studies were not closely correlated with the activity of the drugs *in vivo*. Fuhrman and Field [7] tried to bridge this gap by studying certain homologous series of barbiturates in respect to their chemical structure, physical properties and pharmacological activity. They have shown that as the number of C atoms on the side chain is increased, there is (a) an increase in the ability to inhibit brain respiration, (b) an increase in anaesthetic activity, (c) a decrease in water solubility, and (d) a rise in oil/water coefficient (see fig. 2).

**Distribution and elimination.**—What is really important to establish is the concentration of drug in the brain required to anaesthetize the animal and the concentration which causes depression of brain tissue respiration. If the drug is uniformly distributed in all the tissues of the body, there is no evidence of correlation between the dose of the anaesthetic and the depression of brain tissue respiration. There is good evidence, however, from a variety of investigations on the rat, the rabbit and even the elephant, that after the intravenous administration of certain barbiturates, the concentration of the drug in the brain is about four times that which would be expected on the basis of uniform distribution. Fuhrman and Field [7] have shown that if this preferential distribution is accepted, there is good correlation between inhibition and anaesthetic dose.

It is obvious, however, that the only accurate method of assessment is to determine the actual concentration of the drug in the brain during anaesthesia. When a technique for doing

## SOME PHYSICAL PROPERTIES AND PHYSIOLOGICAL ACTIONS OF SUBSTITUTED 5:5 DERIVATIVES OF BARBITURIC ACID

| Type                               | C atoms side chain | H <sub>2</sub> O solub. gm./lit. | Distrib. coeff. oil/H <sub>2</sub> O | Conc. for 50% inhib. O <sub>2</sub> uptake. Rat brain M × 10 <sup>4</sup> | Delay in onset anaesthesia after I.V.I. mice (mins.) |
|------------------------------------|--------------------|----------------------------------|--------------------------------------|---------------------------------------------------------------------------|------------------------------------------------------|
| 5 Et. : 5 Et. (Barbitone) ..       | 2                  | 6.0                              | 0.214                                | 480.0                                                                     | 22.0                                                 |
| 5 Et. : 5 Isoprop. (Ipral) ..      | 3                  | 1.36                             | 0.73                                 | 130.0                                                                     | 9.2                                                  |
| 5 But. : 5 Et. (Butobarb.) ..      | 4                  | 1.9                              | 2.58                                 | 16.0                                                                      | 1.6                                                  |
| 5 Et. : 5 (1Me. But.) (Pentobarb.) | 5                  | 1.2                              | 4.4                                  | 8.5                                                                       | 0.1                                                  |
| 5 Et. : 5 Iso Amyl. (Amytal) ..    | 5                  | 0.53                             | 2.89                                 | 7.5                                                                       | 0.2                                                  |
| 5 Et. : 5 Hex. (Cyclobarb.) ..     | 6                  |                                  |                                      | 4.0                                                                       | 0.0                                                  |

FIG. 2.—From Fuhrman and Field [7].

this is devised, it should then be possible to determine if anaesthesia occurs at a common level of inhibition, or if the level of inhibition is related to the individual type of drug.

The volatile anaesthetics depend chiefly for their absorption and excretion on the pulmonary ventilation, the blood flow through the lungs, and the partial pressure of the anaesthetic. In the case of the non-volatile anaesthetics which are given by intravenous injection or by other routes, the inactivation of the drug and its subsequent excretion by the kidneys is most important. I shall consider briefly some of the factors involved in controlling the effects of certain barbiturates.

The barbiturates which are used for anaesthesia are usually restricted to those which have a relatively short duration of action. The factors upon which short duration of action depend are unknown though it may be of some significance that such compounds have either long side chains or are sulphur analogues. In contrast to the longer acting compounds, they are excreted in very small amounts in the urine, their action is not prolonged by nephrectomy, and they disappear rapidly from the blood. Koppányi [8], Cameron [9] and others have shown that their duration of action is much longer in animals with liver damage. It has been assumed by some that the drugs are inactivated by the liver but there is no convincing evidence by what means, if any, this is brought about.

Shideman and his colleagues [10], using various techniques for impairing the function of the liver in mice and rats, have confirmed the results of the previous workers, but have thrown little light on the subject.

## SUMMARY

It is possible to say that certain chemical substances, by virtue of their physical properties, gain access preferentially to the cells or cell surfaces of the central nervous system and interfere with those metabolic processes of the brain which are concerned with the utilization of glucose and the synthesis of acetylcholine. The blood flow in the brain being greater than that to most other tissues, contributes, at least initially, to the selectivity of the drug for cerebral tissue.

The interference with brain metabolism is temporary and reversible, except when the drug is used in very high concentration. It is not known whether there is any quantitative relationship between the extent of this interference and the concentration of a particular anaesthetic; nor is it known whether certain centres in the brain are more sensitive than others. The action of the short-acting barbiturates may be prolonged by morphine, phenacetin, anti-histamine substances and also by certain types of liver damage, but the mechanism by which this is effected remains obscure. Mystery also surrounds the variations in susceptibility of different animal species to barbiturates.

## REFERENCES

- 1 LÁZLÓ, D., URBAN, H., and WEISSENBERG, E. (1935) *Arch. exp. Path. Pharm.*, **179**, 266.
- 2 HANDLEY, C. A., SWEENEY, H. M., and BROOKMAN, B. T. (1941) *Proc. Soc. exp. Biol. N.Y.*, **48**, 670.
- 3 QUASTEL, J. H., and WHEATLEY, A. H. M. (1932) *Proc. Roy. Soc.*, **112B**, 60.
- 4 JOWETT, M., and QUASTEL, J. H. (1937) *Biochem. J.*, **31**, 565; (1937) *Biochem. J.*, **31**, 1101.
- 5 GREIG, M. E. (1946) *J. Pharmacol.*, **87**, 185.
- 6 — (1947) *J. Pharmacol.*, **91**, 317.
- 7 FUHRMAN, F. A., and FIELD, J. (1943) *J. Pharmacol.*, **77**, 392.
- 8 KOPPANYI, T., DILLE, J. M., and LINEGAR, C. R. (1936) *J. Pharmacol.*, **58**, 119.
- 9 CAMERON, G. R., and DE SARAM, G. S. W. (1939) *J. Path. Bact.*, **48**, 49.
- 10 SHIDEMAN, F. E., KELLY, A. R., and ADAMS, B. J. (1947) *J. Pharmacol.*, **91**, 331.

Mr. Gordon C. Knight: *Barbiturate anaesthesia in small animals.*—Prior to 1931 when, in the U.S.A., Kreutzer, Haigler and Sweebe and others first employed nembutal in veterinary

surgery, general anaesthesia in small animals, apart from a short period during which avertin gave promise of something new, necessitated the veterinary surgeon's use of chloroform, ether or their mixture almost entirely. As one who well remembers the very frequent difficulties and sometimes disasters which accompanied or followed anaesthesia induced by such methods with or without pre-narcosis, it is no exaggeration to say that barbiturate anaesthesia has so far provided one of the greatest advances in the whole veterinary field. It should not be assumed, however, that the veterinary surgeon may not, on occasions, still usefully employ the older and the newer inhalation anaesthetics, alone or in support of barbiturates; but barbiturate anaesthesia has conferred a boon on the small animal patient and the veterinary surgeon. Through the work carried out on animal anaesthesia by my erstwhile professor and colleague J. G. Wright the way was paved for what is now its almost general use as an anaesthetic for small animals, by the veterinary surgeons of this country.

For general surgery in the dog nembital in average doses  $1/5$  grain per lb. (29 mg. per kilo) body-weight is found to be suitable for non-debilitated and non-toxic animals of about 20 to 40 lb. Outside this range there is some tendency for dosage requirements to decrease slightly as weight increases and increase slightly as weight decreases. For example according to Wright's recommendations in his book "Veterinary Anaesthesia", a dog weighing 60 lb. (27 kg.) needs only 9 grains (583 mg.) not 12 grains (777 mg.), while the dog weighing 10 lb. (4.5 kg.) would probably need  $2\frac{1}{2}$  grains (162 mg.). In practice this applies in a proportion of cases but individual idiosyncrasy is sometimes met and the particular susceptibilities of certain breeds have to be taken well into account.

Nembital can be administered to dogs by the mouth, in gelatine capsules and on an empty stomach anaesthesia can be anticipated within thirty minutes. By injection intraperitoneally of an aqueous solution containing 1 grain (64.8 mg.) per c.c., the onset of anaesthesia is generally obtained within a shorter period. The route of election, however, is intravenous and, by slow injection, the required dose can be assessed on loss of reflexes. About one-quarter to one-third of the dose is injected fairly quickly and the remainder spread over two to three minutes. The effect nembital has upon dogs depends of course upon the dosage. In sub-surgical anaesthetic levels there is considerable variation and certain dogs, notably greyhounds, are not unlikely to develop hyperaesthesia, sometimes of a violent nature. For this reason, particularly in the larger breeds of dogs, it is always wise to have a capable and experienced assistant who can not only exercise adequate control over the animal, but, at the same time, raise a vein by finger pressure and keep the limb firmly extended. Hyperaesthesia from sub-anaesthetic dosage is perhaps, apart from *overdosage*, one of the main factors in the use of nembital against which the veterinary surgeon needs to be on his guard; but, with some experience, one is able to judge by type and temperament when the patient will need unusually careful watching. A fully-grown frenzied and half-anaesthetized dog, even if only medium sized, can present very considerable difficulty. Thus nembital, while holding a unique position as a general anaesthetic for a wide range of animals, is not reliable as an hypnotic.

The development of surgical anaesthesia is usually characterized by one or two enquiring turns of the dog's head, relaxation of musculature and slumping. When first recumbent the animal sometimes moves the limbs in a running motion for a brief period or, with effort, raises the head only promptly to become fully recumbent again. The respirations return to normal after some initial suppression and the pulse, in the average healthy subject, is not markedly affected. The corneal reflex weakens until finally lost while the pupil contracts fully.

A practical and reliable guide to depth of anaesthesia is obtained by sharply pinching the interdigital web. Failure to produce reaction indicates the surgical level has been reached and that, for the time being at any rate, the animal has received a maximal dose. Complete relaxation of glossal and masseter muscles is another useful indication of good depth anaesthesia.

In most surgical cases anaesthesia can then be expected to persist for about an hour. In this respect there is considerable individual variation but in practice I have found that the slower the intravenous administration of nembital the more prolonged its action. This to me has been even more evident with pentothal and comparable barbiturates intended for short duration anaesthesia, the effects of which I have found in most dogs may be very usefully predetermined by the rate of injection.

Sub-surgical anaesthetic levels in small animals are seldom if ever desirable. The veterinary surgeon so often needs his patient anaesthetized, not necessarily for surgery, but for a variety of examinations which would otherwise be difficult simply because the patient is an animal. As a general rule whatever the purpose of the anaesthetization, a safe good depth is an advantage.

Air blockage *without overdosage* and respiratory failure *from overdosage*, are dangers which sometimes have to be met, but with experience it should be very infrequently.

Air blockage can develop when the epiglottis, as so commonly happens in the anæsthetized dog, passes into the nasopharynx with relaxation of the soft palate. The mishap is most common in the bulldog and flat-faced breeds generally. Intubation in such animals should be a matter of routine, in fact with any small animal under barbiturate anæsthesia the precaution is always desirable.

Respiratory failure from overdosage is sometimes sudden in onset but much more commonly follows a progressive shallowness and slowing of respirations. From *slight* overdosage the emergency may occur within five to ten minutes of the dose having been given, and lethal doses injected rapidly for euthanasia can be made to produce the effect almost immediately. A suitable barbiturate in sufficient quantity intravenously thus provides the most æsthetically unobjectionable method of destroying certain animals.

Nembutal and pentothal anæsthesia is indicated in small animals for all major or minor surgical interferences with few exceptions other than *Cæsarian section* where fœtuses are required to survive. Nembutal in this operation results in a very high percentage of deaths in the newly born. Apart from this operation barbiturate anæsthesia has a wide application but its support with ether is often necessary.

Occasionally, in both dogs and cats, the administration of nembutal, and sometimes pentothal, is followed by an unusually long period of coma. The greyhound for example has been known to remain in a semi-comatose condition for up to twenty-four hours after intravenous pentothal, while a dog of any other breed, but with the same dose per unit body-weight, would be fully recovered within about an hour or less.

Similar conditions of prolonged coma from what is presumably delayed detoxication arise very often if a second dose of nembutal or pentothal is given to supplement a first dose. This course needs to be taken with extreme care, particularly with nembutal.

Wherever possible it is better to support nembutal at least with ether rather than give a second intravenous dose of a barbiturate however carefully the dose is assessed on effect.

Both nembutal and pentothal administered *subcutaneously* in small animals are dangerous and can produce deep coma lasting up to two days or more. In some such cases of barbiturate poisoning a large proportion of the dose intended to be given intravenously may have escaped subcutaneously and the animal's restoration has been *impossible* in spite of every form of stimulation, including repeated intravenous injections of picrotoxin producing periods of violent convulsions but only some temporary lightening of the coma.

Although from clinical observation nembutal has no marked depressant cardiac action in small animals, enlargement of the spleen, often to as much as about four times its normal size, is a common feature when full anæsthetic doses are given to the dog. Abdominal palpation of these animals, immediately after the onset of nembutal anæsthesia, often shows the spleen to have folded itself in half longitudinally in the process of its enlargement.

In conclusion I should like to add that evidence of the freedom of nembutal and pentothal from delayed and cumulative toxic action in the average dog has been given on many occasions when animals have received as many as 8 or 9 full anæsthetic doses within fourteen days without apparent untoward effect.

The very simple clinical observations which I have outlined are based upon an average of about 1,000 or more cases of surgical anæsthesia annually since 1943.

Professor G. R. Cameron discussed the action of barbiturates with special reference to liver function and certain constitutional disturbances such as changes in body environment, hæmorrhage, local cooling, fasting, application of tight abdominal bandage and disturbance of the sex hormones.

He reminded members of a Paper he had contributed to the Section of Anæsthetics (1938, *Proc. R. Soc. Med.*, 32, 309) in which these factors were considered and he went on to describe in some detail recent work carried out in his department in conjunction with his colleagues, Drs. G. H. Cooray and S. N. De. He said that these recent experiments had demonstrated the relationship between the male sex hormone, testosterone, and the activity of quick-acting barbiturates such as nembutal, and he proposed the hypothesis linking up the sex hormone with a detoxication mechanism in the liver. The methods used in this investigation were described in some little detail and this led to consideration of the part played by the liver in dealing with sex hormones.

Professor Cameron urged that caution be exercised at present in attributing to the liver only the property of destroying barbiturates and he told of some recent work which had been done in his laboratory by Dr. G. V. R. Born on this important matter. Born has shown that the usually accepted methods of estimating barbiturates in tissues are not free from serious objections and cannot be considered as sensitive. He has worked out a new method which is about 50 to 300 times as sensitive as previous tests and he proposes to reinvestigate the subject of barbiturate absorption, distribution and detoxication by means of this new advance.

## Section of Otology

President—R. SCOTT STEVENSON, F.R.C.S.Ed.

[March 4, 1949]

### “Nerve” Deafness: Its Clinical Criteria, Old and New

By M. R. DIX, C. S. HALLPIKE and J. D. HOOD

*(Aural Department and Otological Research Unit, Medical Research Council, National Hospital, Queen Square, London, W.C.1)*

ACCORDING to the classical precepts which have long governed the functional tests of hearing, the tuning fork tests of Schwabach, Rinne and Weber make it possible to effect a reasonably clear-cut distinction between nerve or perceptive deafness, as it is often termed, and deafness due to disease of the sound-conducting mechanism of the middle ear.

All otologists are trained in the use of these tests for this differential diagnosis, and few would question their value, but to this must be added that one limitation in particular has long been apparent, namely, that while the tests, which may be called the old criteria of nerve deafness, make it possible to diagnose its existence they do not make it possible to go further and say what, and in what way, particular components of the perceptive mechanism have been affected.

During the last ten years, this situation has shown some change for the better. In the first place more information is available concerning the pathological anatomy of the inner ear and eighth nerve. In addition, new knowledge of cochlear function has led to the development of new test procedures. These may be called the *new* criteria of nerve deafness and, as will be seen, they give good promise of enabling us to achieve what the old criteria do not, namely, to add to the diagnosis of nerve deafness some insight into the nature and localization within the perceptive mechanism of the pathological process concerned.

The new criteria which form the subject of this communication are, firstly, the Loudness Recruitment Test and, secondly, the intelligibility test for amplified speech. These tests have been systematically applied in two groups of subjects: firstly Ménière's disease of the labyrinth, and secondly, eighth nerve neurofibroma; and the results obtained will be described and discussed. These two groups have been selected since they exhibit in their pathological anatomy that very difference to which we look to provide a test of our diagnostic criteria. In one group, Ménière's disease, there is good reason to believe that the disturbance of cochlear function is due to an affection of Corti's organ. In neurofibroma, on the other hand, it is known that there occurs a degeneration of the cochlear nerve fibres.

The pathology of eighth nerve neurofibroma has been well described by Cushing (1917), Henschen (1915) and others, and particular mention must be made of the observations of Hardy and Crowe (1936) upon the early stages of its development. The tumours fill the internal auditory meatus, and bring about a gradual pressure destruction of the fibres of the eighth nerve with resulting deafness and loss of the vestibular responses. A point of particular interest is the degeneration of the spiral ganglion within the cochlea, although Corti's organ is as a rule well preserved, a point which has also been established with particular clarity in the case of experimental section of the eighth nerve in animals. These studies are of particular importance since the vastly superior methods of fixation which are possible in animals establish beyond any doubt the anatomical integrity of the hair cells of Corti's organ which follows a lesion of the eighth nerve.

It can therefore be said in summary that neurofibroma of the eighth nerve leads to diffuse degeneration of the fibres of the cochlear nerve with preservation of Corti's organ. This

statement must be amplified in one important respect. If the neurofibroma or operation of eighth nerve section interferes with the blood supply of the cochlea, then Corti's organ is affected, and various degrees of necrosis are to be seen in it and in other cochlear structures.

In the case of Ménière's disease, as the term is now used, there is found a very different state of affairs. The primary change within the labyrinth is a distension of the endolymph system. This has been found in all of the 5 cases which we have had the opportunity of examining, and it has been found, too, in at least a dozen cases examined by other observers. Many of these have described Corti's organ as being normal, but in 3 of our own cases very striking changes have been present.

Figs. 1 and 2 show Corti's organ in 2 of these cases. In fig. 1 the cells have undergone a striking compression and Corti's tunnel is occupied by a structureless coagulum. In fig. 2 the same striking compression of the cell mass is to be seen. In addition the normal staining differentiation between cytoplasm and nuclei has been obliterated.



FIG. 1.

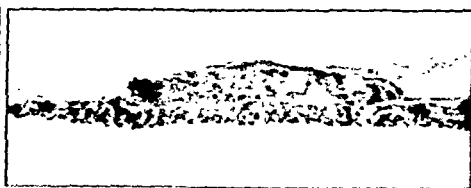


FIG. 2 (By permission of the Editor, *The Annals of Otolaryngology and Rhinology*.)

No doubt can be entertained concerning the significance of this change in Corti's organ in these 2 and in 1 other of our cases, and their importance would appear to be very great. For a full discussion of these changes and their relationship to the deafness of Ménière's disease, reference should be made to a previous communication (Dix *et al.*, 1948).

It is important to add that in none of our cases have we observed any changes in the peripheral cochlear nerve fibres, or in the cells of the spiral ganglion.

In summary it can be said that while in many cases of Ménière's disease the organ of Corti may appear normal, nevertheless, in such cases there are likely to be present certain sub-microscopic residua of the gross changes revealed in 3 of our cases, and it is to these sub-microscopic changes that must be attributed the deafness which in Ménière's disease persists between the attacks. In short, therefore, we are able to say that in eighth nerve neurofibroma the anatomical structures affected are the cochlear nerve fibres, the hair cells being preserved, while in Ménière's disease there occurs a primary affection of the hair cells with preservation of the cochlear nerve fibres.

The results of the classical tuning fork tests, the old criteria, reveal little to distinguish these two groups. In unilateral Ménière's disease Weber's test is typically referred to the normal hearing ear. Rinne's test may give a false negative result if carried out without masking of the normal ear. With masking, however, such a negative result is nearly always reversed. For the measurement of perception by bone conduction we find it best to use the so-called Absolute Bone Conduction Test, with occlusion of the meatus both of the subject and of the examiner. With this test reduced perception is the rule in Ménière's disease, although here again it is necessary to stress the importance of masking the normal ear.

In eighth nerve neurofibroma, these three tests give substantially the same results. With Weber's test, perception is referred to the normal ear, Rinne's test is positive in the affected ear with reduction of perception with the Absolute Bone Conduction Test. There are some exceptions to this rule in which a true negative Rinne appears to be present in the affected ear, and we hope in a later communication to provide more detailed information upon this apparent anomaly.

For the purpose of the present paper, however, it can be taken that the classical tuning-fork tests in eighth nerve neurofibroma, as in Ménière's disease, yield the conventional picture of so-called nerve or perceptive deafness. In other words, although different anatomical components of the perceptive mechanism are affected in these two groups of subjects, the diagnostic recognition of this difference is not possible by means of these old criteria.

Consideration may next be given to the new criteria and, in particular, the manner in which they succeed where the old criteria fail.

*The Loudness Recruitment Test.*—This has been described by its originator, Fowler of New York (1936), by Steinberg and Gardner (1937) and others. We have also described it briefly in our previous communication (Dix *et al.*, 1948). It is still not as well known as it



deserves to be, and for this reason a further brief outline of the test procedure and its rationale may not be out of place.

The application of the test procedure is shown in fig. 3. The subject wears a pair of telephone receivers, each supplied by a separate pure-tone audiometer, or preferably by a single audiometer with arrangements for independent adjustment of the intensity in the two receivers. The frequency of the sound stimulus is the same in each receiver, and the tester switches it alternately from left to right. The purpose of the test is to ascertain and mark upon the ladder diagram two series of intensity levels, one for the right ear and one for the left, each intensity level for the right ear being connected across the diagram with the level for the left ear found by experiment to give a sensation of equal loudness.

The figures given on the diagram represent decibels above the normal threshold. The subject is a normal one, and equal intensities above threshold give equal loudness sensations in the two ears. The rungs of the ladder, therefore, lie horizontally from bottom to top.

In fig. 4 are shown side by side with those of a normal subject the audiograms and loudness

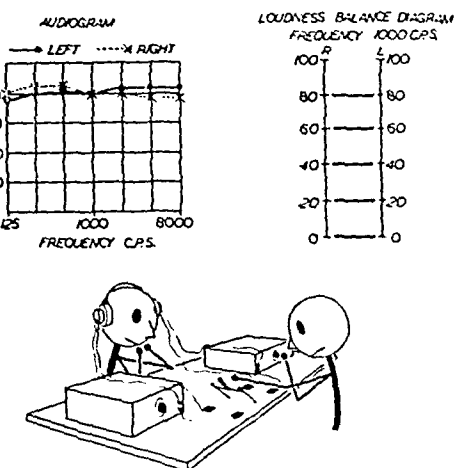


FIG. 3.

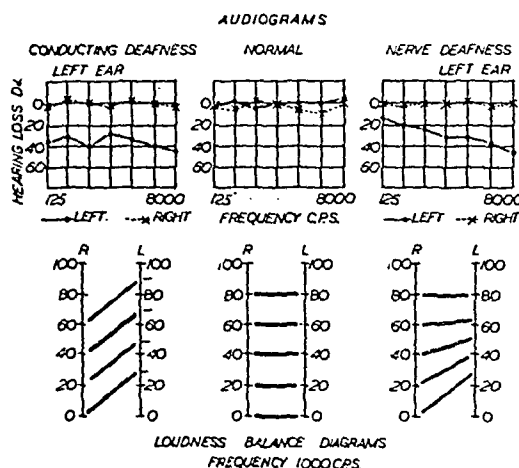


FIG. 4.

recruitment diagrams of two typical cases of unilateral deafness. On the left the deafness is due to a lesion of the conducting mechanism of the middle ear, and on the right to Ménière's disease affecting the left labyrinth. In each case the test frequency selected is 1,000 cycles, at which point the audiogram shows a threshold shift for the affected ear of 30 db. The result obtained in the case of conductive deafness indicates that the loss of sensitivity of the affected ear, 30 db. at threshold, remains constant at 30 db. throughout the entire intensity range. This finding is an unvarying one in conductive deafness, and is explained on the straightforward assumption that the obstruction caused by middle-ear disease to the sound waves on their way to the inner ear introduces an attenuation factor—in this case 30 db.—which is constant at all intensities.

A very different result is obtained in the case of nerve deafness. The audiogram is substantially the same with a threshold shift at 1,000 c/s of 30 db. The balancing points at threshold are identical with a 30 db. displacement upwards for the L. ear. On ascending the intensity scale, however, it is found that the sensitivity loss or deafness of the left ear, 30 db. at threshold, becomes progressively less until at 80 db. equal intensities at the two ears evoke equal loudness responses.

In other words, the deafness of the affected ear present at threshold disappears at higher intensities, and this, in its simplest terms, constitutes the phenomenon of loudness recruitment.

There is general agreement by all who have since investigated the loudness recruitment phenomenon that it is absent in deafness due to uncomplicated middle-ear disease, so-called conductive deafness. On the other hand, it has frequently been demonstrated in a wide variety of disorders of the internal ear and cochlear nerve, including Ménière's disease, which are collectively described as "nerve deafness" and it has come, therefore, to be regarded in a somewhat uncertain manner as a valuable indication of "nerve deafness", using the term in the same wide sense connoted by the old tuning-fork tests.

The results of the Loudness Recruitment Test in Ménière's disease and eighth nerve neurofibroma can be stated very simply.

statement must be amplified in one important respect. If the neurofibroma or operation of eighth nerve section interferes with the blood supply of the cochlea, then Corti's organ is affected, and various degrees of necrosis are to be seen in it and in other cochlear structures.

In the case of Ménière's disease, as the term is now used, there is found a very different state of affairs. The primary change within the labyrinth is a distension of the endolymph system. This has been found in all of the 5 cases which we have had the opportunity of examining, and it has been found, too, in at least a dozen cases examined by other observers. Many of these have described Corti's organ as being normal, but in 3 of our own cases very striking changes have been present.

Figs. 1 and 2 show Corti's organ in 2 of these cases. In fig. 1 the cells have undergone a striking compression and Corti's tunnel is occupied by a structureless coagulum. In fig. 2 the same striking compression of the cell mass is to be seen. In addition the normal staining differentiation between cytoplasm and nuclei has been obliterated.

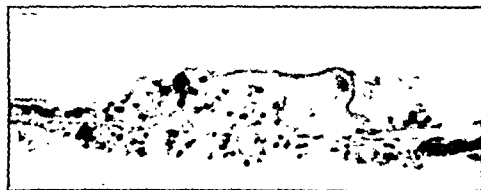


FIG. 1.

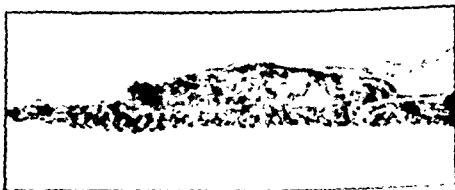


FIG. 2 (By permission of the Editor, *The Annals of Otolaryngology and Rhinology*.)

No doubt can be entertained concerning the significance of this change in Corti's organ in these 2 and in 1 other of our cases, and their importance would appear to be very great. For a full discussion of these changes and their relationship to the deafness of Ménière's disease, reference should be made to a previous communication (Dix *et al.*, 1948).

It is important to add that in none of our cases have we observed any changes in the peripheral cochlear nerve fibres, or in the cells of the spiral ganglion.

In summary it can be said that while in many cases of Ménière's disease the organ of Corti may appear normal, nevertheless, in such cases there are likely to be present certain sub-microscopic residua of the gross changes revealed in 3 of our cases, and it is to these sub-microscopic changes that must be attributed the deafness which in Ménière's disease persists between the attacks. In short, therefore, we are able to say that in eighth nerve neurofibroma the anatomical structures affected are the cochlear nerve fibres, the hair cells being preserved, while in Ménière's disease there occurs a primary affection of the hair cells with preservation of the cochlear nerve fibres.

The results of the classical tuning fork tests, the old criteria, reveal little to distinguish these two groups. In unilateral Ménière's disease Weber's test is typically referred to the normal hearing ear. Rinne's test may give a false negative result if carried out without masking of the normal ear. With masking, however, such a negative result is nearly always reversed. For the measurement of perception by bone conduction we find it best to use the so-called Absolute Bone Conduction Test, with occlusion of the meatus both of the subject and of the examiner. With this test reduced perception is the rule in Ménière's disease, although here again it is necessary to stress the importance of masking the normal ear.

In eighth nerve neurofibroma, these three tests give substantially the same results. With Weber's test, perception is referred to the normal ear, Rinne's test is positive in the affected ear with reduction of perception with the Absolute Bone Conduction Test. There are some exceptions to this rule in which a true negative Rinne appears to be present in the affected ear, and we hope in a later communication to provide more detailed information upon this apparent anomaly.

For the purpose of the present paper, however, it can be taken that the classical tuning-fork tests in eighth nerve neurofibroma, as in Ménière's disease, yield the conventional picture of so-called nerve or perceptive deafness. In other words, although different anatomical components of the perceptive mechanism are affected in these two groups of subjects, the diagnostic recognition of this difference is not possible by means of these old criteria.

Consideration may next be given to the new criteria and, in particular, the manner in which they succeed where the old criteria fail.

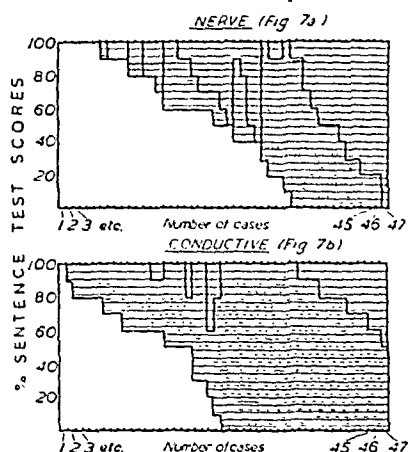
*The Loudness Recruitment Test.*—This has been described by its originator, Fowler of New York (1936), by Steinberg and Gardner (1937) and others. We have also described it briefly in our previous communication (Dix *et al.*, 1948). It is still not as well known as it

with and without hearing aids. In all cases lip-reading was excluded. Disability or deafness for tête-à-tête conversation was rated at nil when 100% of the sentences were understood. When none of the sentences was understood, the disability was rated at 100%. Further tests were then carried out with hearing aids, and the degree of improvement ascertained. The results are shown graphically in fig. 7.

In fig. 7A each case is represented by one of the small sections along the base-line. There are 47 in all. The sentence percentage scores are ranged along the vertical axis. The clear area represents hearing, i.e. percentage of sentences understood, while the hatched area represents deafness or percentage of sentences not understood. The hatched area which is stippled represents the amount of deafness compensated by means of a hearing aid. It will be noted for example that the first 5 cases understood 100% of the sentences and had, therefore, no disability.

At the other end of the scale, Case 47 has a disability of 100% unaided, and regained none of this with a hearing aid. The impression gained from the figure is of a rather large clear area indicating an initial deafness which is not very severe. Secondly, of a rather small stippled area, indicating a rather small amount of improvement with hearing aids.

In fig. 7b, however, a different state of affairs is observed, namely, a much smaller clear area and a much larger stippled area. These results are expressed quantitatively in fig. 8



FIGS. 7A and 7B.

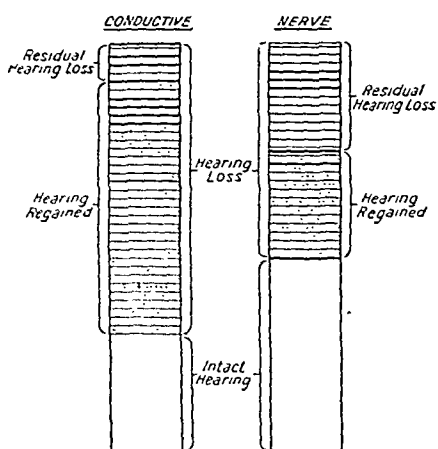


FIG. 8.

which shows that in the case of conductive deafness the unaided hearing capacity, "intact hearing" is small and that practically all of the hearing loss is regained by means of hearing aids, leaving only a small fraction which may be termed residual hearing loss.

With nerve deafness, however, the unaided hearing capacity is very much larger, but comparatively little of the hearing loss is regained and the residual hearing loss is quite considerable.

It may, therefore, be said of these findings that they illustrate very well the truth of the generally accepted belief that deafness lends itself readily to alleviation by means of hearing aids when it is due to disease of the middle ear, but much less readily when it is due to disease of the nervous mechanism of the internal ear or cochlear nerve.

A further point which calls for consideration is the belief generally held by otologists that the pure-tone audiogram and the capacity to understand speech tend to be quite differently related in nerve deafness and in conductive deafness, and in this respect also a comparative study was made of the same two groups of subjects. For the evaluation of the pure-tone audiometric losses, we have made use of a development of the Sabine Percentage Hearing Loss Chart recommended by the American Medical Association (1942). This is shown in fig. 9. The values inscribed in each column are cumulative from above downwards. Thus, the value for the percentage of total hearing loss contributed by the hearing loss at any one of the four frequencies, 512, 1024, 2048 or 4096 cycles/sec. can be read directly from the chart, the figure in question being given in the square immediately above the level at which the hearing loss curve crosses the column concerned. Addition of the four cumulative values then gives the total percentage loss.

In fig. 5 are shown the audiograms of 3 cases of Ménière's disease, with their loudness recruitment diagrams. It will be seen that in every case the sensitivity loss at threshold of the affected ear is completely eliminated at high intensities. In the third case well-marked over-recruitment is seen; that is to say at high intensities the loudness function of the affected ear exceeds that of the normal ear.

In fig. 6 are shown the audiograms in 3 cases of eighth nerve neurofibroma with their

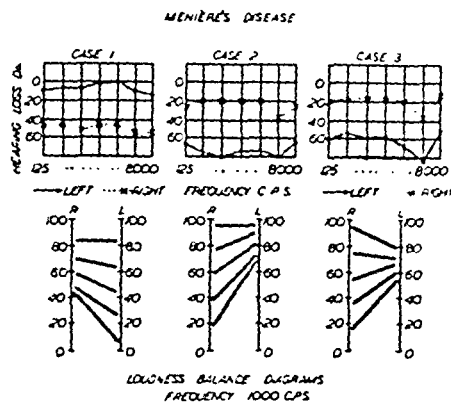


FIG. 5.

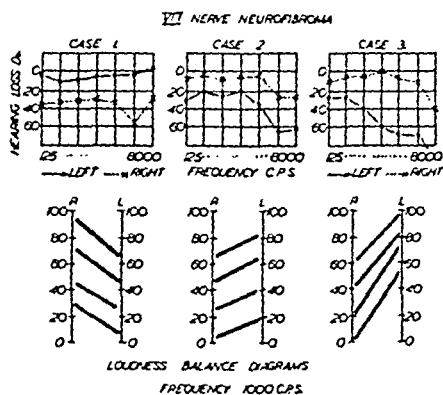


FIG. 6.

loudness recruitment diagrams. It will be seen that in all 3 the sensitivity loss of the affected ear at threshold is maintained at all intensity levels and this is the result generally found in degeneration of the cochlear nerve due to eighth nerve neurofibroma. In a few cases, partial recruitment is found to occur and to this we shall refer again. In only 1 case have we encountered complete recruitment.

Summarizing these findings, it can be said that in Ménière's disease with disorder of the hair cells loudness recruitment is always present. It is generally complete, and over-recruitment is not very uncommon. In eighth nerve neurofibroma, however, loudness recruitment, hitherto described as being uniquely distinctive of nerve deafness, is characteristically not present at all. Instead, there occurs a type of response which is much more in accordance with that found in middle-ear deafness.

In a proportion of cases, however, an incomplete degree of recruitment is found to be present. This we think likely to be due to some degeneration of the hair cells, secondary to involvement of the cochlear blood supply by tumour pressure.

It will therefore be seen that the first of the new criteria, the Loudness Recruitment Test generally makes possible a clear distinction between nerve deafness due to disease of the end-organ and nerve deafness due to disease of the cochlear nerve fibres.

Consideration may next be given to the second of the new criteria.

*The Intelligibility Test for amplified speech.*—Otolologists have for many years been much interested in the way in which deaf patients vary in their ability to hear speech and to understand it. In general they have come to recognize that in nerve deafness, as assessed by the old criteria, inability to understand speech tends to be out of proportion to the threshold sensitivity loss or deafness. This means, in effect, that while such patients hear the sounds of speech, their capacity to understand them is disappointingly low. With conductive deafness, however, this disproportion between hearing and understanding is not present. If, in fact, the sounds of speech can be made to reach the cochlea at all, they seem in general to be well understood.

Otolologists have also come to recognize that in the former group, restoration of intelligibility, as, for example, by means of hearing aids, tends to be inadequate. In the latter group, however, hearing aids are generally very successful in restoring intelligibility.

The validity of these two important beliefs is illustrated by the results of two investigations we were able to carry out at Queen Square in 1945 in the course of work carried out on behalf of the Electro-Acoustics Committee of the Medical Research Council.

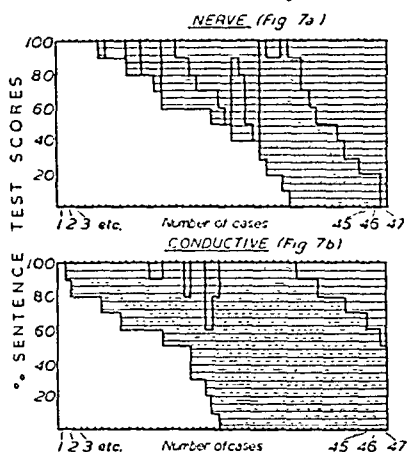
From our clinical material 47 cases were selected in which the tuning-fork tests yielded an unambiguous picture of nerve or perceptive deafness, and another 47 in which these tests were equally clear in indicating conductive or middle-ear deafness. Otoscopic and other investigations were in agreement with the results of the tuning-fork tests. A direct investigation was then carried out of the subject's capacity to understand speech by means of the Fry-Kerridge sentence tests spoken in an ordinary conversational voice at 3 ft. both

with and without hearing aids. In all cases lip-reading was excluded. Disability or deafness for tête-à-tête conversation was rated at nil when 100% of the sentences were understood. When none of the sentences was understood, the disability was rated at 100%. Further tests were then carried out with hearing aids, and the degree of improvement ascertained. The results are shown graphically in fig. 7.

In fig. 7A each case is represented by one of the small sections along the base-line. There are 47 in all. The sentence percentage scores are ranged along the vertical axis. The clear area represents hearing, i.e. percentage of sentences understood, while the hatched area represents deafness or percentage of sentences not understood. The hatched area which is stippled represents the amount of deafness compensated by means of a hearing aid. It will be noted for example that the first 5 cases understood 100% of the sentences and had, therefore, no disability.

At the other end of the scale, Case 47 has a disability of 100% unaided, and regained none of this with a hearing aid. The impression gained from the figure is of a rather large clear area indicating an initial deafness which is not very severe. Secondly, of a rather small stippled area, indicating a rather small amount of improvement with hearing aids.

In fig. 7B, however, a different state of affairs is observed, namely, a much smaller clear area and a much larger stippled area. These results are expressed quantitatively in fig. 8



FIGS. 7A and 7B.

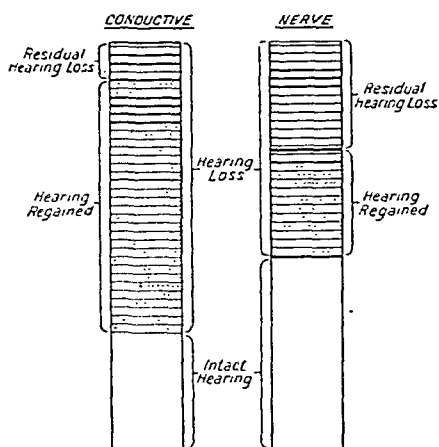


FIG. 8.

which shows that in the case of conductive deafness the unaided hearing capacity, "intact hearing" is small and that practically all of the hearing loss is regained by means of hearing aids, leaving only a small fraction which may be termed residual hearing loss.

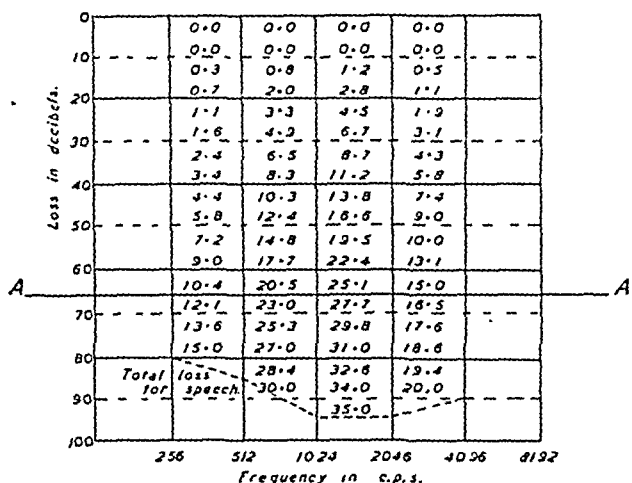
With nerve deafness, however, the unaided hearing capacity is very much larger, but comparatively little of the hearing loss is regained and the residual hearing loss is quite considerable.

It may, therefore, be said of these findings that they illustrate very well the truth of the generally accepted belief that deafness lends itself readily to alleviation by means of hearing aids when it is due to disease of the middle ear, but much less readily when it is due to disease of the nervous mechanism of the internal ear or cochlear nerve.

A further point which calls for consideration is the belief generally held by otologists that the pure-tone audiogram and the capacity to understand speech tend to be quite differently related in nerve deafness and in conductive deafness, and in this respect also a comparative study was made of the same two groups of subjects. For the evaluation of the pure-tone audiometric losses, we have made use of a development of the Sabine Percentage Hearing Loss Chart recommended by the American Medical Association (1942). This is shown in fig. 9. The values inscribed in each column are cumulative from above downwards. Thus, the value for the percentage of total hearing loss contributed by the hearing loss at any one of the four frequencies, 512, 1024, 2048 or 4096 cycles/sec. can be read directly from the chart, the figure in question being given in the square immediately above the level at which the hearing loss curve crosses the column concerned. Addition of the four cumulative values then gives the total percentage loss.

In the case of an audiometric loss represented by the line A—A' the total percentage loss would be given by addition of the figures immediately above the line: 10.4, 20.5, 25.1 and 15.

This method of arriving at a percentage evaluation of hearing loss from a pure-tone audiogram has considerable advantages over any earlier method of this kind. It is, however, still open to the objection that it deals only with threshold intensities and its results, therefore



Total Hearing Loss for Subject with Audiogram  
A—A'  
 $= 10.4 + 20.5 + 25.1 + 15.0 = 71\%$

FIG. 9.—Pure tone audiometer chart for evaluating percentage hearing loss (as approved by the Council on Physical Therapy, American Medical Association).

are not likely always to be related to the behaviour of the ear at intensities well above threshold. Direct measurement of speech intelligibility at different intensity levels is, therefore, a method which we have come to find indispensable.

The method we have employed was devised in connexion with the work of the Electro-Acoustics Committee of the Medical Research Council (1947). The patient is seated with the ear under test at a fixed distance from a loud speaker. Recorded lists of words are then reproduced on the speaker by means of an amplifier system. The method used for recording the results is shown in fig. 10. The amplification can be adjusted within the range of 100 db. and an intensity level at the ear of the listener corresponding to that of the conversational voice at 3 ft. is obtained with an amplifier setting at 50 db. Other settings specified on the

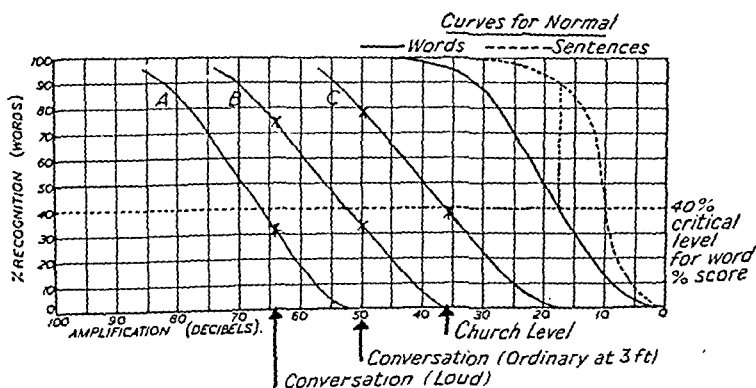


FIG. 10.

chart correspond to the loud conversational voice at 3 ft. This is obtained at 64 db. and the so-called church level at 36 db. The response curves of a normal subject are shown on the right of the chart. At a setting of 30 db. (well below church level) the score would be 90%. At 17 db. the score would be 40% of words corresponding with the 90% point of the sentence intelligibility curve. This 40% score for words is a very critical level since understanding of sentences falls off precipitously at any point below it, as shown by the curve. Thus, if it is desired to know the hearing efficiency of any subject at any of these three levels, church, ordinary conversation or loud conversation, it is required only to know whether at these levels the subject's word score is above or below the critical 40% level.

The curves A, B and C are obtained from three different subjects with varying degrees of deafness.

*Subject A.*—Score with ordinary conversation, nil. Score with loud conversation below the critical level.

*Subject B.*—Score with loud conversation well above the critical level; and with ordinary conversation just below the critical level.

*Subject C.*—Score for ordinary conversation well above the critical level; at church level, just below the critical level.

In all cases the loss for speech is concisely expressed by the displacement of the curve to the left of the normal, as measured along the critical 40% level.

In Case A, this displacement is 50 db. In Case B, 35 db. and in Case C 18 db.

The results of the comparative study in our two groups of subjects of speech audiometry carried out in the manner described and of pure-tone audiometry evaluated in the manner of Sabine, is shown in fig. 11 in the form of a scattergram. As already stated, the otological findings in one group including the tuning-fork tests were characteristic of middle-ear deafness, and in the other, of "nerve" or perceptive deafness.

In fig. 11 the percentage losses as derived by the Sabine method from the pure-tone

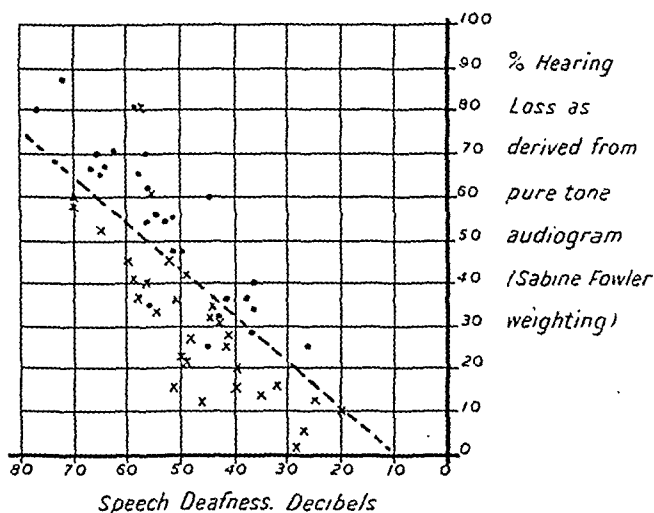


FIG. 11.—Key: Conductive deafness . . . • Nerve deafness . . . x

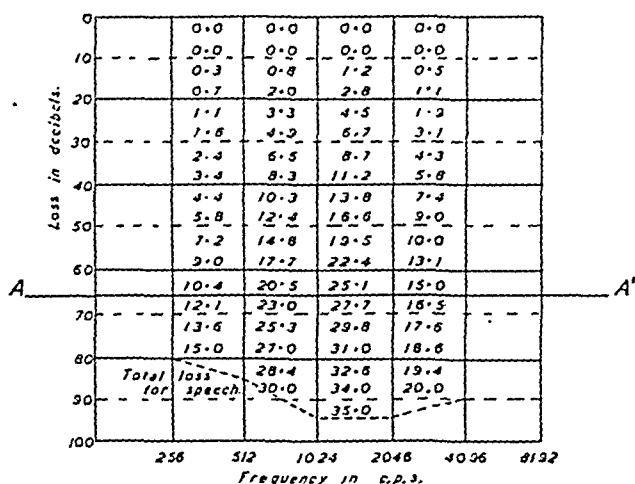
audiogram are plotted along the vertical axis, while speech deafness in decibels is plotted along the horizontal axis.

The distribution of the two groups of symbols reveals a systematic differentiation. Each of the vertical columns bounded by successive ordinates can be regarded as a particular grade of speech deafness. In each such column the symbols are widely distributed, dots lying well above the crosses. In other words, a particular grade of speech deafness is compatible with a degree of pure-tone deafness which tends to be higher if it is due to a middle-ear lesion than to a nerve lesion.

Conversely, each horizontal band of the chart may be regarded as a particular grade of pure-tone deafness. In each such band, the dots or middle-ear symbols are well to the right of the crosses or nerve symbols. In other words, in any one grade of pure-tone deafness the deafness for speech tends to be less if it is due to a middle-ear lesion than to a nerve lesion. These results confirm and systematize the generally-held belief that without knowledge of the pathological basis of the deafness, i.e., whether it is of the "conductive" or "nerve"

In the case of an audiometric loss represented by the line A—A' the total percentage loss would be given by addition of the figures immediately above the line: 10.4, 20.5, 25.1 and 15.

This method of arriving at a percentage evaluation of hearing loss from a pure-tone audiogram has considerable advantages over any earlier method of this kind. It is, however, still open to the objection that it deals only with threshold intensities and its results, therefore



*Total Hearing Loss for Subject with Audiogram*

$$A \text{---} A' \\ = 10.4 + 20.5 + 25.1 + 15.0 = 71\%$$

FIG. 9.—Pure tone audiometer chart for evaluating percentage hearing loss (as approved by the Council on Physical Therapy, American Medical Association).

are not likely always to be related to the behaviour of the ear at intensities well above threshold. Direct measurement of speech intelligibility at different intensity levels is, therefore, a method which we have come to find indispensable.

The method we have employed was devised in connexion with the work of the Electro-Acoustics Committee of the Medical Research Council (1947). The patient is seated with the ear under test at a fixed distance from a loud speaker. Recorded lists of words are then reproduced on the speaker by means of an amplifier system. The method used for recording the results is shown in fig. 10. The amplification can be adjusted within the range of 100 db. and an intensity level at the ear of the listener corresponding to that of the conversational voice at 3 ft. is obtained with an amplifier setting at 50 db. Other settings specified on the

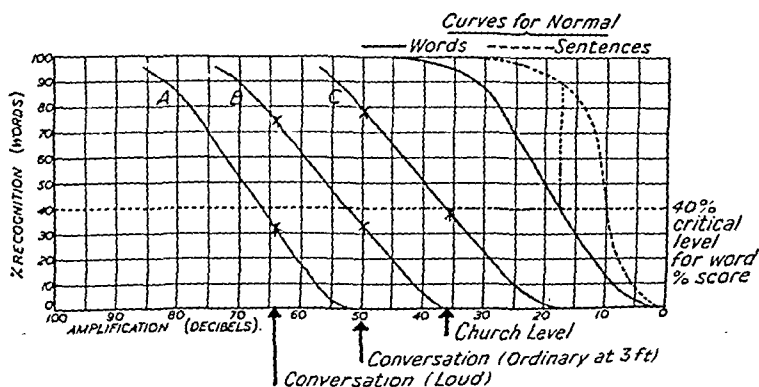


FIG. 10.



chart correspond to the loud conversational voice at 3 ft. This is obtained at 64 db. and the so-called church level at 36 db. The response curves of a normal subject are shown on the right of the chart. At a setting of 30 db. (well below church level) the score would be 90%. At 17 db. the score would be 40% of words corresponding with the 90% point of the sentence intelligibility curve. This 40% score for words is a very critical level since understanding of sentences falls off precipitously at any point below it, as shown by the curve. Thus, if it is desired to know the hearing efficiency of any subject at any of these three levels, church, ordinary conversation or loud conversation, it is required only to know whether at these levels the subject's word score is above or below the critical 40% level.

The curves A, B and C are obtained from three different subjects with varying degrees of deafness.

*Subject A.*—Score with ordinary conversation, nil. Score with loud conversation below the critical level.

*Subject B.*—Score with loud conversation well above the critical level; and with ordinary conversation just below the critical level.

*Subject C.*—Score for ordinary conversation well above the critical level; at church level, just below the critical level.

In all cases the loss for speech is concisely expressed by the displacement of the curve to the left of the normal, as measured along the critical 40% level.

In Case A, this displacement is 50 db. In Case B, 35 db. and in Case C 18 db.

The results of the comparative study in our two groups of subjects of speech audiometry carried out in the manner described and of pure-tone audiometry evaluated in the manner of Sabine, is shown in fig. 11 in the form of a scattergram. As already stated, the otological findings in one group including the tuning-fork tests were characteristic of middle-ear deafness, and in the other, of "nerve" or perceptive deafness.

In fig. 11 the percentage losses as derived by the Sabine method from the pure-tone

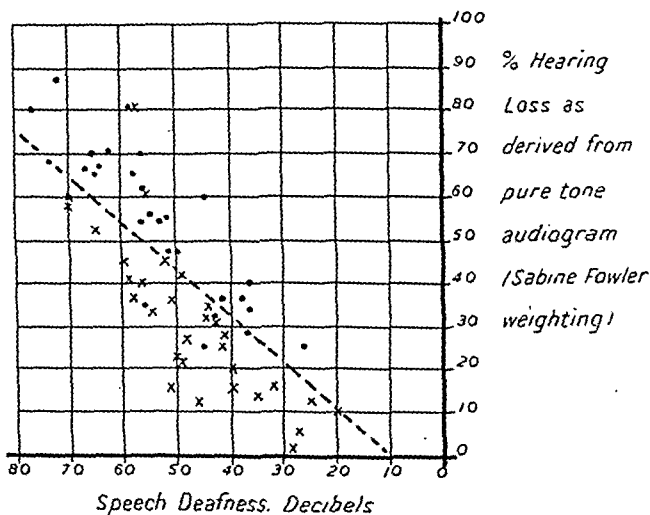


Fig. 11.—Key: Conductive deafness . . . • Nerve deafness . . . ×

audiogram are plotted along the vertical axis, while speech deafness in decibels is plotted along the horizontal axis.

The distribution of the two groups of symbols reveals a systematic differentiation. Each of the vertical columns bounded by successive ordinates can be regarded as a particular grade of speech deafness. In each such column the symbols are widely distributed, dots lying well above the crosses. In other words, a particular grade of speech deafness is compatible with a degree of pure-tone deafness which tends to be higher if it is due to a middle-ear lesion than to a nerve lesion.

Conversely, each horizontal band of the chart may be regarded as a particular grade of pure-tone deafness. In each such band, the dots or middle-ear symbols are well to the right of the crosses or nerve symbols. In other words, in any one grade of pure-tone deafness the deafness for speech tends to be less if it is due to a middle-ear lesion than to a nerve lesion. These results confirm and systematize the generally-held belief that without knowledge of the pathological basis of the deafness, i.e., whether it is of the "conductive" or "nerve"

type, pure-tone audiometric findings cannot reliably be related to the hearing capacity for speech. They exemplify, too, the general truth of the belief that in nerve deafness, as assessed by the old criteria, loss of intelligibility for speech tends to be disproportionately larger than the pure-tone audiometric loss, and tends also to be disproportionately larger and more difficult to compensate by means of hearing aids. This does not, however, apply to all of our cases of "nerve" deafness as will readily be seen from the situation of some of the x symbols in the scattergram, and a closer analysis of the anatomical basis of our cases of "nerve" deafness has, therefore, been attempted by means of systematic application of the speech audiometric tests in two groups of subjects in whom the deafness was due respectively to Ménière's disease and eighth nerve neurofibroma.

In fig. 12 is shown, for comparison, the unaided and aided speech audiogram of two cases of middle-ear deafness.

In Case A the speech deafness as measured at the critical level is 61 db. It will also be noted that the unaided curve lies approximately parallel to the normal curve, a point of considerable importance.

The aided curve shows very substantial displacement to the right, towards the normal unaided curve, the speech deafness, in fact, being reduced to 27 db.

With Case B a similar result is obtained. The unaided curve is of normal contour. It is displaced some 40 db. to the left of the normal curve. With an aid the speech deafness is reduced to 16 db. As would be expected, the aided curves reproduce in both cases the form of the unaided curves.

In fig. 13 are shown the very different results obtained in two cases of Ménière's disease. The unaided curves do not lie parallel to the normal curve. Both shown a downward slope towards the left, indicating a disproportionate failure of intelligibility with amplification. With hearing aids, although the unaided curves are displaced to the right, their form is unchanged and the improvement in intelligibility is disappointingly small. Thus in neither case is there obtained a word percentage score for ordinary conversation which is above the critical 40% level. Both of these cases were typical of Ménière's disease in showing complete loudness recruitment and it can thus be said of Ménière's disease that while recruitment of loudness is the rule, recruitment of intelligibility, which might be expected, may be conspicuously absent. *In fact, the opposite would appear to occur, namely, that as loudness increases intelligibility falls off.*

We come, finally, to speech audiometry in cases of nerve deafness due to eighth nerve neurofibroma. The results of speech audiometry in 2 cases of nerve deafness due to eighth nerve neurofibroma are shown in fig. 14.

In both cases, the unaided and aided curves lie parallel to the normal as shown in fig. 12. With all four curves intelligibility continues to improve with amplification up to high levels and in both cases it is possible to bring the percentage score for ordinary conversation well above the critical 40% level.

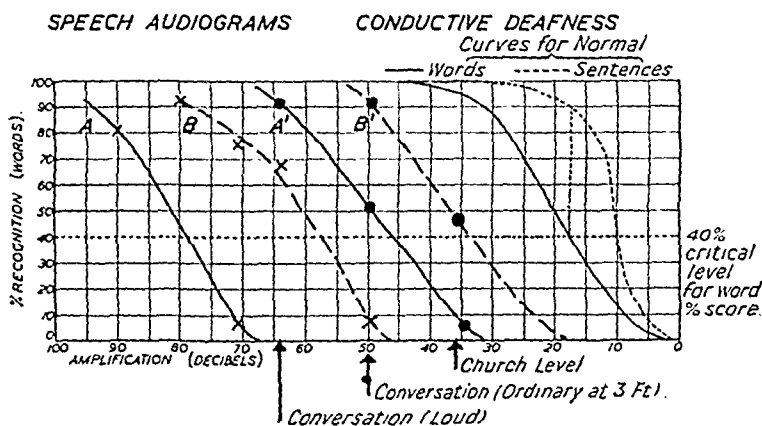
It will be seen therefore that as with the first of our new criteria, so with the second. Quite different results are obtained in end-organ lesions and in nerve-fibre lesions. Both, therefore, succeed where the old criteria fail, in making clear the important distinction between these two conditions.

The principles which underlie the use of these new criteria for so useful an analysis of the anatomical basis of nerve deafness, are still far from being well understood. In certain particulars too, the facts themselves cannot yet be regarded as well established. This applies in particular to the reactions to amplified speech which are encountered in Ménière's disease. Speech audiometric curves, having the form displayed in fig. 13, though highly characteristic of this disorder, are by no means always present. Indeed, some subjects of Ménière's disease, particularly in its quiescent phases, derive considerable benefit from hearing aids, although here, again, they practically all show a marked unwillingness to use these instruments, a clinical fact which is perhaps more distinctive of the condition than the results of audiometric or indeed any tests.

It is necessary finally to emphasize the remarkable way in which, both with the Loudness Recruitment Tests and with speech audiometry, the results obtained in nerve-fibre lesions approximate to those obtained in lesions of the conducting mechanism of the middle ear.

Some explanation for this resemblance has been offered in our previous discussion of the loudness recruitment phenomenon (Dix *et al.*, 1948) and it is hoped that further light will be thrown upon it by the results of investigations at present in progress.

Clinically, the resemblance is of great practical importance, and helps to explain the serious diagnostic error which is still encountered of mistaking an early eighth nerve neurofibroma for early unilateral otosclerosis.



|        | Speech deafness (Decibels) | Unaided | Aided |
|--------|----------------------------|---------|-------|
| Case A | .. .. .                    | 61      | 27    |
| Case B | .. .. .                    | 40      | 16    |

FIG. 12.—Speech audiograms. Conductive deafness.

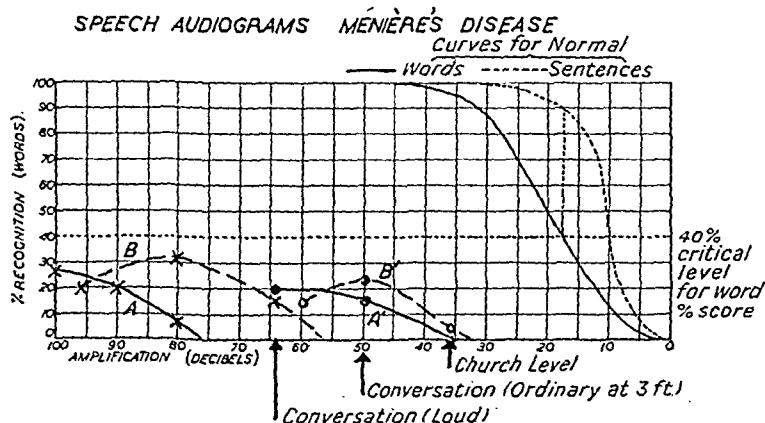
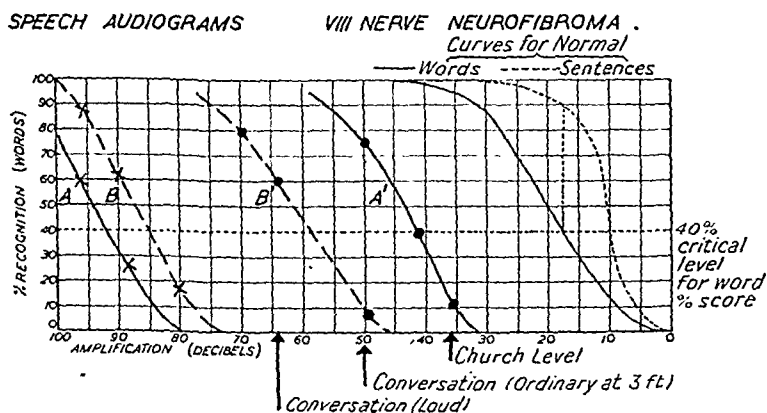


FIG. 13.—Speech audiograms. Ménière's disease.



|        | Speech deafness (Decibels) | Unaided | Aided |
|--------|----------------------------|---------|-------|
| Case A | .. .. .                    | 75      | 25    |
| Case B | .. .. .                    | 67      | 41    |

FIG. 14.—Speech audiograms. Eighth nerve neurofibroma.

type, pure-tone audiometric findings cannot reliably be related to the hearing capacity for speech. They exemplify, too, the general truth of the belief that in nerve deafness, as assessed by the old criteria, loss of intelligibility for speech tends to be disproportionately larger than the pure-tone audiometric loss, and tends also to be disproportionately larger and more difficult to compensate by means of hearing aids. This does not, however, apply to all of our cases of "nerve" deafness as will readily be seen from the situation of some of the x symbols in the scattergram, and a closer analysis of the anatomical basis of our cases of "nerve" deafness has, therefore, been attempted by means of systematic application of the speech audiometric tests in two groups of subjects in whom the deafness was due respectively to Ménière's disease and eighth nerve neurofibroma.

In fig. 12 is shown, for comparison, the unaided and aided speech audiogram of two cases of middle-ear deafness.

In Case A the speech deafness as measured at the critical level is 61 db. It will also be noted that the unaided curve lies approximately parallel to the normal curve, a point of considerable importance.

The aided curve shows very substantial displacement to the right, towards the normal unaided curve, the speech deafness, in fact, being reduced to 27 db.

With Case B a similar result is obtained. The unaided curve is of normal contour. It is displaced some 40 db. to the left of the normal curve. With an aid the speech deafness is reduced to 16 db. As would be expected, the aided curves reproduce in both cases the form of the unaided curves.

In fig. 13 are shown the very different results obtained in two cases of Ménière's disease. The unaided curves do not lie parallel to the normal curve. Both shown a downward slope towards the left, indicating a disproportionate failure of intelligibility with amplification. With hearing aids, although the unaided curves are displaced to the right, their form is unchanged and the improvement in intelligibility is disappointingly small. Thus in neither case is there obtained a word percentage score for ordinary conversation which is above the critical 40% level. Both of these cases were typical of Ménière's disease in showing complete loudness recruitment and it can thus be said of Ménière's disease that while recruitment of loudness is the rule, recruitment of intelligibility, which might be expected, may be conspicuously absent. In fact, the opposite would appear to occur, namely, that as loudness increases intelligibility falls off.

We come, finally, to speech audiometry in cases of nerve deafness due to eighth nerve neurofibroma. The results of speech audiometry in 2 cases of nerve deafness due to eighth nerve neurofibroma are shown in fig. 14.

In both cases, the unaided and aided curves lie parallel to the normal as shown in fig. 12. With all four curves intelligibility continues to improve with amplification up to high levels and in both cases it is possible to bring the percentage score for ordinary conversation well above the critical 40% level.

It will be seen therefore that as with the first of our new criteria, so with the second. Quite different results are obtained in end-organ lesions and in nerve-fibre lesions. Both, therefore, succeed where the old criteria fail, in making clear the important distinction between these two conditions.

The principles which underlie the use of these new criteria for so useful an analysis of the anatomical basis of nerve deafness, are still far from being well understood. In certain particulars too, the facts themselves cannot yet be regarded as well established. This applies in particular to the reactions to amplified speech which are encountered in Ménière's disease. Speech audiometric curves, having the form displayed in fig. 13, though highly characteristic of this disorder, are by no means always present. Indeed, some subjects of Ménière's disease, particularly in its quiescent phases, derive considerable benefit from hearing aids, although here, again, they practically all show a marked unwillingness to use these instruments, a clinical fact which is perhaps more distinctive of the condition than the results of audiometric or indeed any tests.

It is necessary finally to emphasize the remarkable way in which, both with the Loudness Recruitment Tests and with speech audiometry, the results obtained in nerve-fibre lesions approximate to those obtained in lesions of the conducting mechanism of the middle ear.

Some explanation for this resemblance has been offered in our previous discussion of the loudness recruitment phenomenon (Dix *et al.*, 1948) and it is hoped that further light will be thrown upon it by the results of investigations at present in progress.

Clinically, the resemblance is of great practical importance, and helps to explain the serious diagnostic error which is still encountered of mistaking an early eighth nerve neurofibroma for early unilateral otosclerosis.

In connexion with the cases of occupational causes and the gunfire and explosion causes, it is interesting to refer to recent views on the theories of hearing. Reboul [7] considered the hydrodynamics of the propagation of a fluid wave within small conical cavities. He computed the movements of these waves within such tiny elongated cavities as the scala vestibuli and scala tympani. He maintains that the pressure waves and waves of elongation set up by each tone is a function of the vibratory frequency of that tone. Such waves will impinge upon the reception endings of the organ of Corti at specific points. The point of impingement in the cochlea of a given wave can be calculated mathematically. This theory makes it unnecessary to assume that thousands of little microphones are lined up in the cochlea waiting for the tones to locate them. On the contrary, fluid vibrations at a given frequency will always produce sufficient pressure at a mathematically predictable point to set into action a relatively simple perceptive mechanism. Much more proof of these propositions is, of course, needed. But there is some experimental support for it, e.g. Larsell's [5] histological studies of the developing cochlea of the pouched opossum embryo, from which movement reflexes and oscillographic responses were secured only as various areas reached functional activity. In discussing these findings, one of the joint authors of the paper, McCrady, comes to the same conclusions as Reboul. McCrady [5] puts it this way: "The maximum efficiency of pressure exerted by the energy of sound wave travelling through a liquid in a tube, depends upon the relation of wavelength to the circumference of the tube."

He found that by mathematical calculation he could expect a certain area of the cochlea to be receptive to the precise sounds which, from other experimental evidence, such as Hallpike's, we believe are received there. This theory may well explain the mechanism by which sound waves reach the appropriate area of the cochlear mechanism and set off the stimulus which is interpreted in the cortex by us as the sound corresponding to that stimulus. But it does not explain why sounds of varying pitch but of great intensity, or of varying pitch but of sustained and lesser intensity, i.e. the conditions producing occupational deafness, &c., all tend to produce the lesion in the cochlea which we have come to refer to as "the 4096 dip". On the basis of this theory we should expect to find the lesion in occupational deafness and gunfire, &c., at the point in the cochlea where we believe the pitch involved is received by the cochlea. It seems to me that there must be some other explanation of the "4096 dip" commonly found in traumatic cases. Here I would point out that this "dip" is not confined to traumatic cases. It is also found in many cases of chronic otitis media of long-standing, where there has been no associated trauma. Is there an explanation common to both causes, i.e. other than trauma?

(3) *Vascular causes.*—First let me mention the cases in this group which I think you will accept without question. They are:

|                           | No. of cases |
|---------------------------|--------------|
| Ménière's disease.. ..    | 10           |
| Arteriosclerosis .. ..    | 15           |
| Anæmia .. ..              | 1            |
| Cerebral thrombosis .. .. | 1            |
| Thyrotoxicosis .. ..      | 1            |
|                           | <hr/> 28     |

The next group, 16 cases, are those which are attributed to the results of chronic otitis media. In support of my contention that these are vascular in origin I would quote Eggston and Wolff [2]:

"No inner ear appears microscopically perfectly normal in the presence of a well-established otitis media. Dean and Bunch on the basis of audiometer records gave clinical evidence of this fact . . . Clinically the hearing and vestibular functions return to normal when the otitis has been cured, as a general rule."

It is my belief that the 16 cases here mentioned, were, for various reasons, caused by vascular changes in the cochlea as a result of vascular changes in the middle-ear from old chronic otitis media. If we accept these as being of vascular origin, then we have a total, so far, of 44.

There are still 9 cases of syphilis to classify. We assume that some of the cases will show cochlear changes due to an endarteritis obliterans and some will show trophic changes in the nerve. If, for the purpose of this discussion, we say that 4 out of the 9 cases show endarteritis obliterans, we have now a total of 48 cases out of 100 in which the vascular changes are the primary cause of the perceptive deafness.

I want to acknowledge here my indebtedness to Professor Harris [4] of the Anatomy School, University of Cambridge. It was he who drew my attention to some of the anomalies in the accepted ideas of the vascular supply of the cochlea.

Sunderland [8] has drawn attention to the fact that the exact size of the internal auditory artery, in relation to the other structures in the internal auditory meatus, is rarely appreciated.

## REFERENCES

- Council on Physical Therapy. American Medical Association (1942) *J. Amer. med. Ass.*, 119, 1108.  
 CUSHING, H. (1917) *Tumours of the Nervus Acusticus*. Philadelphia and London.  
 DIX, M. R., HALLPIKE, C. S., and HOOD, J. D. (1948) *Proc. R. Soc. Med.*, 41, 516.  
 FOWLER, E. P. (1936) *Arch. Otolaryng.*, Chicago, 24, 731.  
 HARDY, M., and CROWE, S. J. (1936) *Arch. Surg.*, Chicago, 32, 292.  
 HENSCHEN, F. (1915) *Arch. Psychiat.*, 56, 21.  
*Med. Res. Council. Spec. Rep. Ser.* (1947) No. 261 Hearing Aids and Audiometers. H.M.S.O.  
 STEINBERG, J. C., and GARDNER, M. P. (1937) *J. acoust. Soc. Amer.*, 9, 11.

## The Causes of Perceptive Deafness

By R. R. SIMPSON, F.R.C.S.Ed.

I WANT to approach this subject, in the first place, from the clinical aspect. For this purpose I have taken 100 cases of perceptive deafness seen by me during the last year at the Hull Royal Infirmary. All the cases showed the accepted clinical findings, including audiograms both for air and bone conduction. The causes of the deafness were, in my view, as follows:

| Cause                                                      | No. of cases |
|------------------------------------------------------------|--------------|
| (1) Results of chronic otitis media .. .. .                | 16           |
| (2) Traumatic: (a) Gunfire, bomb-blast, explosions .. .. . | 12           |
| (b) Occupational .. .. .                                   | 11           |
| (c) Concussion .. .. .                                     | 5            |
| (d) Fracture of the skull .. .. .                          | 2            |
| (3) Ménière's disease .. .. .                              | 10           |
| (4) Syphilis .. .. .                                       | 9            |
| (5) Arteriosclerosis .. .. .                               | 15           |
| (6) Influenza .. .. .                                      | 4            |
| (7) Measles (without otitis media) .. .. .                 | 2            |
| (8) Paget's disease .. .. .                                | 2            |
| (9) Diphtheria .. .. .                                     | 1            |
| (10) Diabetes .. .. .                                      | 1            |
| (11) Anæmia (hypochromic microcytic) .. .. .               | 1            |
| (12) Mumps .. .. .                                         | 1            |
| (13) Scarlet fever (without otitis media) .. .. .          | 1            |
| (14) Cerebral thrombosis .. .. .                           | 1            |
| (15) Thyrotoxicosis .. .. .                                | 1            |
| (16) Lead poisoning .. .. .                                | 1            |
| (17) Undetermined .. .. .                                  | 4            |
| Total                                                      | 100          |

It is not a comprehensive list. I have excluded, for example, all congenital causes. It is not to enumerate the detailed causes that I show this list. It is rather to consider the primary causes of perceptive deafness as illustrated by such a list. Such a list can be divided into three main primary causes: (a) neuritic; (b) traumatic; (c) vascular.

(1) Cases where the nerve elements of the Perceptive Mechanism are primarily involved, e.g.

|                        |   |
|------------------------|---|
| Influenza .. .. .      | 4 |
| Measles .. .. .        | 1 |
| Diphtheria .. .. .     | 1 |
| Diabetes .. .. .       | 1 |
| Mumps .. .. .          | 1 |
| Scarlet fever .. .. .  | 1 |
| Lead poisoning .. .. . | 1 |

10 cases

In none of these cases was there any evidence of a previous otitis media. The membranes appeared normal and intact. In the history of the case there appeared to me to be a direct connexion between the disease mentioned and the incidence of the deafness. It appeared that these diseases exerted a direct toxic effect on the nerve cells of the cochlea or the nerve itself.

Eggston and Wolff [2] suggest that in the cases of perceptive deafness due to drugs, the lesion is an allergic reaction in the cochlea itself.

(2) *Traumatic causes.*—These cases are divided into 4 groups, roughly on the degree of trauma applied. In the case of the fracture of the skull and concussion (7 cases) the degree of trauma is the most severe. Next come the cases caused by explosions, bomb-blast and gunfire (12 cases). And the least in degree of trauma are those due to various occupations (11 cases).

In connexion with the cases of occupational causes and the gunfire and explosion causes, it is interesting to refer to recent views on the theories of hearing. Reboul [7] considered the hydrodynamics of the propagation of a fluid wave within small conical cavities. He computed the movements of these waves within such tiny elongated cavities as the scala vestibuli and scala tympani. He maintains that the pressure waves and waves of elongation set up by each tone is a function of the vibratory frequency of that tone. Such waves will impinge upon the reception endings of the organ of Corti at specific points. The point of impingement in the cochlea of a given wave can be calculated mathematically. This theory makes it unnecessary to assume that thousands of little microphones are lined up in the cochlea waiting for the tones to locate them. On the contrary, fluid vibrations at a given frequency will always produce sufficient pressure at a mathematically predictable point to set into action a relatively simple perceptive mechanism. Much more proof of these propositions is, of course, needed. But there is some experimental support for it, e.g. Larsell's [5] histological studies of the developing cochlea of the pouched opossum embryo, from which movement reflexes and oscillographic responses were secured only as various areas reached functional activity. In discussing these findings, one of the joint authors of the paper, McCrady, comes to the same conclusions as Reboul. McCrady [5] puts it this way: "The maximum efficiency of pressure exerted by the energy of sound wave travelling through a liquid in a tube, depends upon the relation of wavelength to the circumference of the tube."

He found that by mathematical calculation he could expect a certain area of the cochlea to be receptive to the precise sounds which, from other experimental evidence, such as Hallpike's, we believe are received there. This theory may well explain the mechanism by which sound waves reach the appropriate area of the cochlear mechanism and set off the stimulus which is interpreted in the cortex by us as the sound corresponding to that stimulus. But it does not explain why sounds of varying pitch but of great intensity, or of varying pitch but of sustained and lesser intensity, i.e. the conditions producing occupational deafness, &c., all tend to produce the lesion in the cochlea which we have come to refer to as "the 4096 dip". On the basis of this theory we should expect to find the lesion in occupational deafness and gunfire, &c., at the point in the cochlea where we believe the pitch involved is received by the cochlea. It seems to me that there must be some other explanation of the "4096 dip" commonly found in traumatic cases. Here I would point out that this "dip" is not confined to traumatic cases. It is also found in many cases of chronic otitis media of long-standing, where there has been no associated trauma. Is there an explanation common to both causes, i.e. other than trauma?

(3) *Vascular causes*.—First let me mention the cases in this group which I think you will accept without question. They are:

|                           | No. of cases |
|---------------------------|--------------|
| Ménière's disease .. ..   | 10           |
| Arteriosclerosis .. ..    | 15           |
| Anæmia .. ..              | 1            |
| Cerebral thrombosis .. .. | 1            |
| Thyrotoxicosis .. ..      | 1            |
|                           | <hr/> 28     |

The next group, 16 cases, are those which are attributed to the results of chronic otitis media. In support of my contention that these are vascular in origin I would quote Eggston and Wolff [2]:

"No inner ear appears microscopically perfectly normal in the presence of a well-established otitis media. Dean and Bunch on the basis of audiometer records gave clinical evidence of this fact . . . Clinically the hearing and vestibular functions return to normal when the otitis has been cured, as a general rule."

It is my belief that the 16 cases here mentioned, were, for various reasons, caused by vascular changes in the cochlea as a result of vascular changes in the middle-ear from old chronic otitis media. If we accept these as being of vascular origin, then we have a total, so far, of 44.

There are still 9 cases of syphilis to classify. We assume that some of the cases will show cochlear changes due to an endarteritis obliterans and some will show trophic changes in the nerve. If, for the purpose of this discussion, we say that 4 out of the 9 cases show endarteritis obliterans, we have now a total of 48 cases out of 100 in which the vascular changes are the primary cause of the perceptive deafness.

I want to acknowledge here my indebtedness to Professor Harris [4] of the Anatomy School, University of Cambridge. It was he who drew my attention to some of the anomalies in the accepted ideas of the vascular supply of the cochlea.

Sunderland [8] has drawn attention to the fact that the exact size of the internal auditory artery, in relation to the other structures in the internal auditory meatus, is rarely appreciated.

The reason being that, in the dissection of this area, the brain is lifted up and the attachments cut in order to expose the internal meatus. If, however, the brain is gently retracted, fig. 1 is the picture that is seen. Note, first, the unexpected length of the artery, and secondly, its small calibre when compared to the nerves in the meatus. Sunderland found that in 17% of specimens the internal auditory artery took origin independently from the basilar artery and entered the meatus as a separate arterial channel anterior to the seventh and eighth

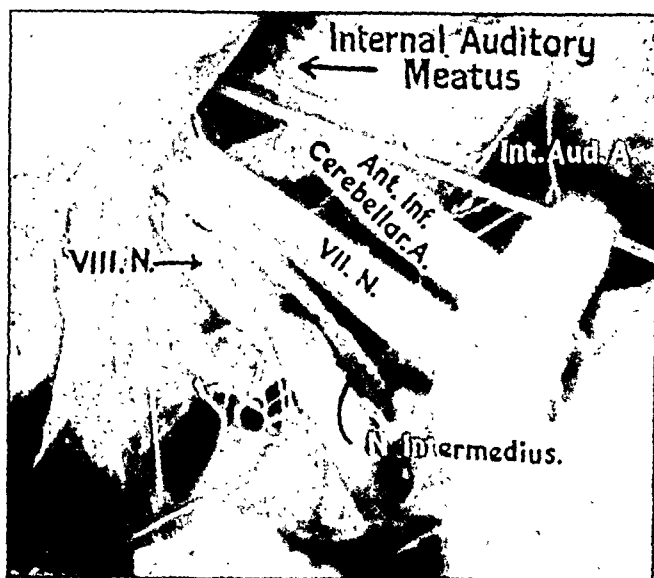


FIG. 1.—After S. Sunderland, *Brain*, 1945, 68, 25. "The arterial relations of the internal auditory meatus."

nerves. In the remaining 83%, the artery took origin from a variable point on the anterior inferior cerebellar artery. The evidence favours, therefore, a predominant origin of the internal auditory artery from the anterior inferior cerebellar artery. When the anterior inferior cerebellar artery passes between the nerves entering the internal auditory meatus, it does so, in most instances, between the main motor division and the portio intermedia.

Sunderland adds that the knowledge of such a relationship is of considerable functional importance in surgical explorations of the cerebellopontine angle and in connexion with certain disturbances of nerve conduction which may possibly arise as a direct consequence of mechanical pressure exerted on the nerves by atheromatous, enlarging, abnormally pulsating or tortuous vessels.

In the internal auditory meatus, this artery gives off a cochleo-vestibular branch, which divides into a trunk supplying the proximal two-thirds of the basal coil of the cochlea, and a posterior vestibular artery. The continuation of the internal auditory artery divides into two trunks, one entering the modiolus and supplying all of the cochlea excepting the proximal two-thirds of the basal coil, and the other the anterior vestibular artery. These branches are all terminal or "end-arteries" constituting the sole blood supply for their respective areas of distribution.

Next, Professor Harris draws attention to the generally accepted or conventional diagrams of the vascular supply of the cochlea in order to contrast them with real specimens. Fig. 2 is taken from Abderhalden. Eggston and Wolff [2], quoting Nabeya and Assia, also accept this arrangement of the vascular supply. Commenting on this, Professor Harris lays down the general principle that whenever an artery goes through a long fibrous canal, it is *not* accompanied by one vein but by a plexus of veins (cf. pampiniform plexus, vertebral venous plexus, &c.). Professor Harris has confirmed this view by examining sections to show the vascular supply in the labyrinth of a ten-and-a-half weeks human embryo. Therefore, in the internal ear one should expect not only arterial phenomena but also venous phenomena, e.g. varicosities, thrombosis, &c.

Concerning the physiology of the vascular supply of the labyrinth, Mygind and Falbe-Hansen [6] maintain that: (a) In contrast to the general reaction of the organism, the



labyrinth shows vasoconstriction after the injection of histamine, vasodilatation after adrenaline, presumably thus compensating the universal change of blood-pressure. (b) The water-binding power of the labyrinthine cells is increased by injections of histamine, lowered by adrenaline.

There is some evidence, therefore, for supposing that the vascular mechanism of the internal ear is designed to counteract sudden changes in the vascular tension of the rest of the body.

I mentioned earlier that Reboul's theory did not explain "the 4096 dip". It will be seen that a vascular lesion would. If we assume, therefore, that in the traumatic causes where a "4096 dip" is found, the lesion is vascular, we can add to the vascular causes a further 23

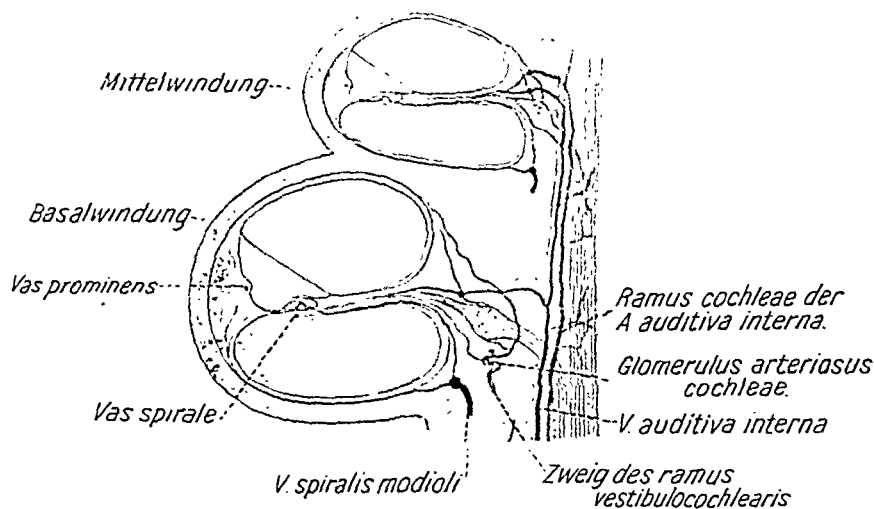


FIG. 2.—Diagram of the distribution of blood vessels in the cochlea. (From Abderhalden.)

cases (12 gunfire, blast, explosion and 11 occupational). This would bring the total of the vascular causes up to 71 out of 100 cases, a figure very much higher than I had previously considered.

The evidence to support this vascular theory, so far as I am aware, is based on clinical grounds and theoretical speculation. I know of no direct experimental evidence to support it.

Asherson [1] in discussing the question, maintains that "any noise above a certain intensity is a stimulus, which reacts through the ear and produces a spasm of an end-artery distributed to that part of the high-tone division of the cochlear nerve which transmits the frequencies 4096". But he does not venture an explanation of how this reflex works. Instead he asks: "Is the original arteriole spasm a reflex via the tympanic membrane and the stapedius muscle? Is this reflex protective in gearing down the conductivity of the nerve to prevent too loud a sound being transmitted?"

These and many other questions must be answered by the evidence of future experiments in this almost unexplored field.

#### REFERENCES

- 1 ASHERSON, N. (1940) *J. Laryng.*, 55, 531.
- 2 EGGSTON, A. A., and WOLFF, D. (1947) *The Histopathology of the Ear, Nose and Throat*. Baltimore, p. 400.
- 3 — (1947) *The Histopathology of the Ear, Nose and Throat*. Baltimore, p. 189.
- 4 HARRIS, H. A. (1948) Personal communication.
- 5 LARSELL, O., MCCRADY, E., and LARSELL, J. F. (1944) *Arch. Otolaryng.*, 40, 233.
- 6 MYGIND, S. H., and FALBE-HANSEN, J. (1946) *Acta Oto-laryng.*, Stockh., 34, 69.
- 7 REBOUL, J. A. (1938) *J. Phys. Rad.*, 9, 185.
- 8 SUNDERLAND, S. (1945) *Brain*, 68, 23.

Mr. E. D. D. Davis asked Mr. Hallpike for his views on the subject of masking, since in his own experience the procedure was often of little clinical value.

Mr. Terence Cawthorne said that with the new concept presented by the authors it was possible clinically by means of these tests to distinguish between a lesion of the end-organ as seen in Ménière's disease and a lesion of the nerve trunk as seen in a neurofibroma. At a neurological hospital such problems were common and they had the experience that the method put forward was of real practical value. He believed that this study would be of great help in differentiating between a lesion of the end-organ and the trunk of the eighth nerve.

Mr. Simson Hall said that he had listened to the Paper read by Dr. Hallpike with great pleasure and profit and congratulated him and his colleagues on the very practical approach which they had adopted towards these problems. He had had the advantage of hearing Dr. Hallpike talking on this subject some time ago in the Section of Neurology, and what he had said that morning put in a more practical and everyday fashion what he had advanced on the previous occasion. He was extremely interested in his speech intelligibility differential test. One question arose on this matter. Dr. Hallpike told them that he was using a loudspeaker for testing. He would like his opinion as to whether he preferred to use live speech or reproduced speech. Would he consider these tests of the same value if carried out with a more crude method? In other words, was it essential to have scientifically graded speech? The speech intelligibility curve which he had shown demonstrated in a graphic form a point which was of interest to those who were dealing with the operative side of the correction of deafness.

There was no doubt that direct assessment of the intelligibility of speech was needed in assessing the value of the fenestration operation. They had found in many cases that although they had got a satisfactory rise in the audiometric chart, the raising of the lower tone limit did not give the patient any real satisfaction, and sometimes his condition was worse than before, because owing to nerve loss, the intelligibility suffered very considerably.

Referring to Mr. Simpson's paper, he was extremely interested in the result of vascular change in otitis media. In a Paper which he himself had read to the Section a little while ago he had pointed out that in early otitis media the nerve change was obvious and was the last thing to recover. He wondered whether they could link that up with some of the vascular changes of which Mr. Simpson had spoken. The same thing occurred after the fenestration operation. Mr. Simpson had certainly given them some new ideas on that subject.

Air Commodore E. D. D. Dickson showed records of cases of perceptive deafness occurring in airmen who had undertaken high altitude diving. None of these experienced pain during the dive. The eustachian tubes were patent and the tympanic membranes were normal in appearance when seen. Audiometric tests showed a perceptive type of deafness and the caloric stimulation of the labyrinth gave a normal response. (These latter findings were checked and corroborated by Hallpike at Queen Square.) The first case dived from 14,000 ft. and the second from 30,000 ft. to 10,000 ft. The third case lost consciousness whilst looping an aircraft and regained it at 3,000 ft. On landing all complained of deafness in one or other ear which has persisted. What was the cause of such deafness? Was it due to pressure changes in the inner ear confined to the cochlea?

Mr. H. V. Forster said that having listened to the discussion, he had been reminded of an old question put to us with anxiety by our deafened patients. Would the use of an electrically powered aid eventually damage the hearing?

Recent contributions by European workers, for example, de Maré, Huizing and Pothoven, renew interest in this question when applied especially to cases of perception deafness associated with the loudness recruitment phenomenon.

He thought it would be agreed that our answer should be definitely encouraging in cases of obstructive or middle-ear deafness, but when the inner-ear system is at fault, the answer must be guarded and be dependent on the improved design of hearing aids.

Certain developments in the design of these instruments are expressed by such terms as "peak clipping" and "compression amplification", but he, Mr. Forster, would not press Mr. Hallpike and his co-workers for information on this technical problem, which he hoped might be discussed at some future meeting of the Section.

Older people are grateful to the practised public speaker and experienced politician, not only for his clear diction, but also for the well-spaced words and sentences. This latter quality, however, is often impatiently criticized by the younger listener.

#### REFERENCES

- DE MARÉ, GÖRAN (1948) *Acta Oto-laryng. Stockh.* Suppl. 74, 107.  
 HUIZING, H. C. (1948) *Acta Oto-laryng. Stockh.*, 36, 346.  
 POTHOVEN, W. J. (1948) *Acta Oto-laryng. Stockh.*, 36, 301.

Dr. C. S. Hallpike in reply to Mr. Davis said that for their own part they paid a great deal of attention to masking, and they found it absolutely essential in many of the cases with which they had to deal. He would not like to say that they yet knew the best way to do it, for the technical difficulties were quite considerable, but he did think it a very important subject indeed.

In answer to Mr. Simson Hall, he did not think they had any objection to live speech, which had certain advantages, but it was a question of time and trouble. The technical difficulties of reproducing speech were now so small that he would have thought that the use of properly recorded speech for this kind of work might be recommended very heartily.

## Section of Urology

President—TERENCE J. MILLIN, M.A., M.Ch., F.R.C.S.

[January 27, 1949]

### Pituitrin Therapy in Hydronephrosis

By J. G. YATES BELL, F.R.C.S.

This paper is based on clinical results and differs in its findings from some recent scientific work.

Lapides (1948) measures the urinary output from one kidney and simultaneously records the contraction rate and pressure of the opposite ureter. In brief his findings are that no drug affects ureteric contractions except by influencing the urinary flow either directly as a diuretic or more indirectly by altering the blood-pressure. In his experiments the effect of pitressin injections was to decrease urinary output and subsequent ureteral activity. The only other influences on ureteric contractions, apart from diuresis, were an increase in abdominal pressure as in straining and an increase in the peripheral resistance in his apparatus.

On the other hand Jona (1936) read a paper before this Section in January 1936 on the kidney pelvis, its normal and pathological physiology which did not receive the attention it deserved. In brief his pyeloscopy consisted in observing on the fluorescent screen the effects of various drugs on the contractions of the renal pelvis and ureter.

He described spasms of the communicating channel between the calix and the infundibulum, which in his opinion was generally reflex from local irritation, bacterial or chemical, or from neighbouring disease, e.g. gall-bladder.

In 1928 Jona showed that pituitrin produced rhythmic contractions followed by relaxation and relief of pain, and stressed the disappearance of anti-peristalsis in a case of cystitis with resulting subsidence of infection. He thought that the kidney pelvis continued to function normally once its function had been restored.

I used pyeloscopy at this time in cases of renal sympathetico-tonus to assess suitability for sympathectomy but soon replaced this rather involved investigation by observing the therapeutic effects of pituitrin,  $\frac{1}{2}$  c.c. of which was given daily for a week or so. There were two ways of assessing benefit, one from the very early relief of renal pain and secondly by the repeat intravenous pyelography which could show a decrease in the spasm; the assumption being that the best inhibition to sphincter spasm is the relaxation which precedes a peristaltic wave.

A typical case is the following (LEH/41/2054): A woman, aged 32, had right-sided pain for years, all investigations normal except that the right renal pelvis was not outlined in the I.V.P. and spasm of the upper calix at first suggested to the X-ray Department a possibility of tubercle. The spasm was overcome at retrograde pyelography and this showed normal pictures (sometimes pain is brought on by the passage of the ureteric catheter or fluid injection which reproduces the patient's symptoms: a valuable diagnostic aid). This patient had a course of pituitrin injections for one week and was "cured" and discharged to have a further course from her own doctor. She has remained well.

A small percentage of renal sympathetico-tonus cases, then, are cured by pituitrin treatment but a large number relapse and, although partly relieved by a second course of treatment, may fail to respond to a third course and need renal sympathectomy to relieve symptoms and prevent development of hydronephrosis.

One very interesting case (36/6540), a girl of 26 years, attended me with four years' history of left-sided pain and pyelitis; the pain was very severe, the *B. coli* infection persistent and the I.V.P. (23.11.36) showed constant imperfect filling of the left renal pelvis. Pyeloscopy failed owing to vomiting and vagal upset. A course of pituitrin  $\frac{1}{2}$  c.c. b.d. in this case was given and the urine was sterile by 8.12.36. Pain was improved but not cured. This rapid cure of previously resistant infection was noticed in many

cases and was attributed to increased peristalsis overcoming the spasm and removing the renal residual urine. The subsequent history of this case was remarkable: The pain relapsing in due course, a sympathectomy was done with relief for two years, when the same condition developed in the other kidney which was not relieved until sympathectomy. Later the patient had her inferior mesenteric ganglion removed for bowel pain, only to develop Raynaud's disease during recent years.

A third case is provided by a patient (35/5934) who had left-sided pain and had been investigated for gastric colic, arthritic and neurological conditions for some years. The urine was sterile and the I.V.P. showed marked spasm in all the left calices while pyeloscopy showed great increase in peristalsis with pituitrin. This patient remained well after pituitrin treatment.

Pituitrin or pitressin has a place in the treatment of these renal sympathetico-tonus cases and the associated chronic pyelitis of some, but in view of the considerable psychological instability of so many, there are likely to be many disappointments; nevertheless it is still often preferable to a sympathectomy in such a case.

This help with infection led me to try pituitrin after uretero-colostomy, particularly in the early weeks after transplantation when considerable atonia or hydronephrosis may be seen in the excretion urogram.

A patient, three weeks after uretero-colostomy in 1942 after failure of eight operations for vesico-vaginal fistula, developed severe pyelitis with hydronephrosis, a course of pituitrin was given, the patient had no further infection and the kidney returned to normal contour.

Another uretero-colostomy for tuberculous systolic bladder in a nephrectomized patient developed renal pain and alarming diminished urinary output twelve days later, presumably due to œdema—as pituitrin relieved the pain and re-established the urinary flow.

On these lines it occurred to me that pituitrin might be of help in the hydronephrosis seen so often in cases of paraplegia. Riches (1943), at Stoke Mandeville, found 77% had urinary infection and a resulting mortality of 14.3% up to two years and a 20% incidence of renal calculi.

After initial causes of death from lung wounds and bed sores, in the later stages urinary failure from infected, dilated kidneys remained the commonest cause of death; this is frequently associated with renal and bladder stones.

H. S. Talbot (1948) of Richmond, Virginia, observed in the U.S.A. 331 paraplegias of whom 16 were known to have hydronephrosis. Of these 13 are alive with hydronephrosis without stones, roughly 5%. Talbot stresses the importance of vesico-ureteral reflux (10 out of 15) in the formation of hydronephrosis in addition to urinary infection and ureteritis, and discusses the value of uretero-neo-cystotomy.

At Leatherhead Emergency Hospital we were fortunate enough to have no renal death and only one case noted of renal stone formation (and this patient did not relapse after operation). This was partly attributed to:

- (1) Use of strong urinary acidifiers. Ammonium nitrate 0.5 gramme 10 a day and Suby's solution G 1 (Acetic acid 0.5% in earlier cases) for bladder washouts.

- (2) Reduction of infection by penicillin, antiseptics, chemotherapy and N.A.B.

- (3) Catheter drainage (Foley) replacing suprapubic cystotomy as far as possible, often for many months and no urethral stricture recorded.

- (4) Regular assessment by I.V.P., particularly the residual urine, urine culture and cystoscopy.

Cystograms were very useful in showing reflux but great care must be taken not to over-distend the bladder as urinary infection is likely to follow. Results were difficult to correlate and just as good by excretion route.

- (5) Pituitrin injections for developing hydronephrosis.

Slides were then shown illustrating the benefit of pituitrin treatment for this type of hydronephrosis. All were 30-minute films. (Figs. 1-10.)



FIG. 1 (CASE I).—Mortar Wound, D7, Oct. 1944. April 1945: Bilateral hydronephrosis and course of pituitrin started.



FIG. 2 (CASE I).—June 1945: Marked improvement in hydronephrosis.



FIG. 3 (CASE I).—Aug. 1946: Bladder capacity now 10 oz., healed and continent for three hours.



FIG. 4 (CASE II).—Gunshot wound, D11, Aug. 1944. Suprapubic cystostomy. 1945: Feb. Myelolysis, cauda equina found completely divided. March. Bladder cap. 4 oz. Bed sores healed. Micturition never satisfactorily established.



FIG. 5 (CASE II).—April 1946: Ten months later vast hydro-ureters, marked hydronephrosis. Course of pituitrin.



FIG. 6 (CASE II).—June 1946: Improvement but left side still dilated. Marked improvement right side. As might be expected, this patient relapsed, but has improved again, clinically as well as radiologically, with pituitrin.



FIG. 7 (CASE III).—Mortar Wound, D7, Oct. 1944. Suprapubic cystotomy. April 1945: Bilateral hydronephrosis and course of pituitrin started.



FIG. 8 (CASE III).—June 1945: Marked improvement in hydronephrosis. In August 1946 the bladder capacity was 10 ounces, healed and continent for three hours. I.V.P. no tendency to return to hydronephrosis.



FIG. 9 (CASE IV).—March 1947: Hydrocalix and hydro-ureter.



FIG. 10 (CASE IV).—After course of treatment upper right calix only shows residual clubbing.

CASE IV.—Figs. 9 and 10 were taken after the war in an officer wounded at Alamein who leads an active life in a wheel chair. He was convinced that he would die of renal failure from hydronephrosis and infection and he refused to get rid of his cystotomy tube which he managed very well but which was probably the cause of his hydronephrosis persisting. Patient remains well and free from bouts of urinary fever but keeps his cystotomy as he fears inability to function properly. Actually nearly all these patients can be healed and taught to pass water as they know when the bladder is full.

(At cystoscopy bladder distension produces sweating above the level of the lesion, as shown by Guttman.) An interesting point in this case is the satisfactory result considering the length of time the hydronephrosis had been known to exist. Rigid and fibrosed as hydroureters and hydronephroses are likely to become mainly after recurrent or chronic infection, length of time itself tends to become an unfavourable factor in estimating prognosis in this type of case.

CASE V.—Shell Wound. D12. August 1944.

Suprapubic cystotomy. Much urinary infection with rigors.

March 1945: Bilateral hydronephrosis. Pituitrin started.

This patient had had a very severe bilateral hydro-ureter and hydronephrosis and was ill for many weeks with a high temperature. He was eventually cured by pituitrin and became well enough to have the small stone removed from the left kidney after healing of the cystotomy wound [Slides shown].

The course of treatment is  $\frac{1}{2}$  c.c. daily for two weeks,  $\frac{1}{2}$  c.c. alternate days for two weeks and a maintenance dose of  $\frac{1}{2}$  c.c. once a week for six weeks.

There is no place for pituitrin in the treatment of "obstructive" hydronephrosis, although it may help in "resolution" after removal of an obstruction, e.g. stone.

Females should be warned to expect excessive menstruation.

The mode of action is not clear but there is no doubt in my mind of its clinical value and the pyeloscopy pictures suggest increased peristalsis as the method. If it were diuresis, surely a drink of water would give equally good results? If it is suggested that by acting on the bladder better drainage is promoted, this cannot apply where the bladder is contracted and empties by cystotomy tube as in Case II.

Another group of cases where pituitrin is likely to be helpful is the hydronephrosis of pregnancy but obviously the uterus and its contents prevent its exhibition; it is very useful after delivery for delay in return to normal of this dilatation; also if there is infection associated with the stagnation.

I have endeavoured to show the value of pituitrin injections for hydronephrosis (and accompanying infection) associated with renal sympathetico-tonus, paraplegia and pregnancy as well as after surgical transplantation. (Do these four not suggest a neuro-sympathetic cause for the hydronephrosis?)

I would like to mention the help I had from Dr. David Allen in investigating and treating these spinal cases.

#### REFERENCES

JONA, LEON (1936) *Proc. R. Soc. Med.*, 29, 623.

— (1928) *Med. J. Austr.*, 2, 118.

LAPIDES, J. (1948) *J. Urol.*, 59, 501.

RICHES, E. (1943) *Brit. J. Surg.*, 31, 135.

TALBOT, H. S. (1948) *J. Urol.*, 59, 1130.

Dr. L. Guttman: Some time ago Mr. Yates-Bell drew my attention to his observations on the beneficial effect of pituitrin in cases with hydronephrosis, and we have studied the effect of this treatment on several paraplegic patients at the Spinal Injuries Centre, Stoke Mandeville. It was found that pituitrin had a markedly beneficial effect in certain cases of unilateral hydronephrosis without raised blood urea. As an example, the case of a patient with a complete transverse lesion at T.4 is described. An I.V.P. in September 1948 revealed a unilateral (left) hydronephrosis. This was confirmed by a cystogram made on November 9, 1948 (fig. 1, A, B), which shows a reflux into a markedly dilated left ureter and a hydronephrotic kidney. Pituitrin was started on November 15, 1948, with daily injections of 1 c.c. at first, but, as this produced severe diarrhoea, it was continued with daily injections of  $\frac{1}{2}$  c.c. only. An I.V.P. a fortnight later showed marked diminution of the hydronephrosis, which was confirmed by a cystogram on December 3, 1948 (fig. 2, A, B). Pituitrin was given until December 12, 1948, and further improvement was found. The treatment was then discontinued, and a cystogram on January 24, 1949, showed that the left kidney and ureter had virtually regained normal size (fig. 3, A, B).

A further case (cauda equina lesion at L.4) is described, in which pituitrin also had a profound beneficial effect on the hydronephrosis. However, when the treatment was discontinued there was a recurrence. A course of pituitrin was, therefore, repeated, and again had a prompt effect. Since then, the patient has been having 1 c.c. pituitrin every three days, and the last I.V.P. on January 22,

1949, showed that the great improvement was still being maintained. No obvious beneficial effect was found in cases with hydronephrosis and long-standing raised blood urea. Although the number of our cases treated with pituitrin is not large enough to allow positive conclusions to be drawn, the results so far obtained are encouraging enough to warrant our carrying out further studies with this treatment.



FIG. 1A.



FIG. 2A.



FIG. 3A.



FIG. 1B.—9.11.48.



FIG. 2B.—3.12.48.



FIG. 3B.—24.1.49.

FIG. 1, A, B.—Cystogram before pituitrin treatment. Reflux into left hydroureter and hydronephrosis.

FIG. 2, A, B.—Cystogram 18 days after pituitrin treatment. Marked diminution of hydronephrosis and hydroureter.

FIG. 3, A, B.—Cystogram 42 days after completion of pituitrin treatment. Normal kidney and ureter.



## The Operative Treatment of Urinary Incontinence in the Male

By G. M. LEWIS, M.B., F.R.C.S.

TRUE incontinence of urine must be distinguished from the overflow of chronic retention, from the urgency of micturition associated with bladder neck irritation or congestion, and from the extreme frequency characteristic of the systolic bladder, holding only a thimbleful of urine. This differentiation should not be difficult.

The cases with which we are primarily concerned are: First, those found in conjunction with malformation of the central nervous system such as spina bifida, and secondly, those due to trauma to the sphincters or their nerve supply.

In practice, the latter, and more important, group resolves itself into the post-prostatectomy cases.

Following prostatectomy, by whatever route, the patient relies for urinary control on his external sphincter only. Transient incontinence is a not infrequent finding when urethral micturition starts again after removal of the gland. This usually clears up in a day or two and is of no significance.

Permanent post-prostatectomy incontinence has been reported, with varying degrees of reluctance, after every type of operation: relatively seldom after suprapubic enucleation, more commonly after perurethral resection, and most of all following the perineal operation. Recently we have seen a few cases, referred from other hospitals, in which the retropubic approach has been used.

Naturally this complication is more likely to occur after a radical prostatectomy, either retropubic or perineal, than after a simple adenectomy.

Following most of these interventions the mode of injury to the external, and only remaining, sphincter is readily understood. There are two ways in which the sphincter can be damaged in the retropubic operation. First, when deliberately sectioning the urethra, the scissors, instead of hugging the apex of the adenoma, are thrust down too far into the region of the membranous urethra before cutting. Secondly, if the urethra is not divided, or if enucleation is too rough, the membranous urethra is avulsed with the adenoma and the tell-tale tag is later seen at the lower end of the specimen. Both these are errors of technique.

Scarring at the apex of the prostatic bed, though rare, can give rise to involuntary leakage of urine in the presence of a normal sphincter. It is important that this condition should be excluded in every case of post-operative incontinence as its treatment is relatively simple. Apical scarring gives rise to stricture formation in the region of the external sphincter, with the symptoms of incontinence and the passage of a thin stream. Paradoxically it rapidly responds to early dilatation which softens up the scar tissue and allows the muscle to function.

It must be remembered that incontinence, like any other symptom, can vary in degree. At one end of the scale is the man who never urinates in quantity but who is continuously dribbling. At the other is the patient with only a slight sphincteric weakness, who leaks a little towards the end of the day when the musculature tires. Somewhere in between these two extremes is found one who is able to pass small quantities of urine, is continent whilst lying in bed, but who dribbles when in an upright position.

Formerly, and all too often nowadays, treatment has been entirely palliative. For complete incontinence—the bag, for the lesser degrees—the penile clamp; both of which are but confessions of failure on the part of modern surgery.

Numerous surgical techniques have been advanced from time to time, with varying degrees of success, three of which aim at constricting the bulbous urethra.

First, the Lowsley-Hunt plication of the bulbo-cavernosus muscle, with ribbon catgut. Now this muscle is often so thin and tenuous that it seems to me most unlikely that any permanent diminution of the urethral calibre can be produced in this way. Secondly, the procedure of Player and Callender, after Giordano, of

lapping the bulb with the gracilis muscle transplanted from the thigh. Thirdly I would refer to the operation introduced by our President, Mr. Terence Millin, in 1938, of surrounding the bulb with ribbon catgut. These last two procedures have had considerable success because they do produce a permanent fibrous constriction around the urethra. (I do not believe that the transplanted muscle can retain any contractility.) However the disadvantage of these operations where the bulbous urethra is completely surrounded, either by muscle, fascia or catgut, is that, whilst the encircling pressure is equally applied to the corpus spongiosum, it is unequally applied to the urethral mucosa, as the latter is not centrally situated within the corpus. Trophic ulceration of the mucosa, with fistula, and, later, stricture formation is liable to occur, particularly in those cases due to spina bifida.

The object of all these operations, including my present one, is the same: to produce an occlusive infolding of the urethral mucosa, supported by the vascular tissue of the corpus spongiosum with its natural elasticity. This is brought about by plication, not of the bulbo-cavernosus muscle, but of the corpus spongiosum itself by means of four or five silk sutures. The plication is carried out over a rubber catheter in the urethra. The size of the catheter should depend, to a certain extent, on the degree of incontinence. For the average case a 15 Ch Tiemann catheter is used. If the incontinence is greater then a catheter of lesser calibre is indicated. The catheter is left in situ for five days and then removed.

[A film demonstrating the operative technique was then shown. This was followed by a slide of a post-operative urethrogram showing the constriction produced in the bulb by the plication sutures.]

This is a minor surgical procedure. It can do no harm and in a large proportion of cases will help to alleviate this most distressing complaint.

[March 24, 1949]

## Vesical Diverticula. [Abridged]

By HOWARD G. HANLEY, M.D., F.R.C.S.

THE subject of vesical diverticula has not been discussed at this Section for many years. In 1935, Mr. Ogier Ward gave his Presidential Address on bladder diverticulum but, apart from several specimens shown at clinico-pathological meetings, we have to go back twenty-six years, to find the last time when the subject was debated (July 1923):

Compared with such subjects as lithiasis, stricture and hydronephrosis, diverticulum of the bladder is only a recently discovered disease, and although Pean in 1895 removed the first diverticulum from a 15-year-old girl, only 5 cases were recorded in the literature up to 1906. Since then there have been several outstanding papers on the subject and many series of cases have been recorded. The majority of the large series published have been collected from the various clinics in America and are the work of several surgeons, so that Mr. Ogier Ward's series of 53 cases published in 1938 is still one of the largest personal collections.

Unfortunately we have no agreed distinction between a very deep sacculation and a very small diverticulum, but in my own operation notes I have always recorded the depth to which a ureteric catheter would pass into the sac, and anything shallower than 2 cm. has been excluded from my 16 cases discussed here.

The recent recognition of the condition is not surprising when we remember that it may cause no symptoms whatever, and has no specific syndrome, and that modern diagnostic aids such as cystoscopy and X-rays which reveal the condition.

### ÆTIOLOGY

Diverticulum is still in doubt, but most people believe that of the bladder wall, some obstructive factor must be present; relief of this obstruction forms an equally important part of treatment.

It is found in women, sometimes without any evidence of obstruction, with fibrous bladder-neck obstruction or benign enlargement, and more than the large adenomatous variety.

Analysing my own cases, there was one female without any evidence of obstruction, but the diverticulum was unquestionably congenital. It opened below the right ureteric orifice and extended upwards and outwards towards the lateral pelvic wall. It was 3 in. long by 1½ in. wide and was joined by a blind-ending tube about 2 in. long which crossed over the common iliac vessels with the right ureter, and which I have assumed to be an accessory blind-ending ureter. Apart from this case, all the others have had evidence of marked urinary obstruction of one sort or another (Table I). There were 7 cases of prostatic ob-

TABLE I.—OBSTRUCTIVE FACTOR IN 16 CASES OF VESICAL DIVERTICULA

|                                           |    |    |    |    |         |
|-------------------------------------------|----|----|----|----|---------|
| Small prostatic adenoma                   | .. | .. | .. | .. | 7 cases |
| Fibrous bladder neck—Cold punch           | 2  | .. | .. | .. | 6 cases |
| Wedge excision                            | 4  | .. | .. | .. |         |
| Urethral strictures                       | .. | .. | .. | .. | 2 cases |
| No obstructive factor. Female. Congenital | .. | .. | .. | .. | 1 case  |

struction, 6 fibrous bladder-neck obstructions (four of which had a wedge excised at the time of the diverticulectomy and two being treated with the cold punch) and 2 very long-standing urethral strictures.

My operation notes indicate that the enucleation was difficult and fibrotic in 5 of the prostatectomies, and this is in keeping with Badenoch's findings in his Hunterian Lecture (1949) when he states that he has not seen a diverticulum in the presence of a large adenomatous prostate.

A diverticulum *per se* gives no characteristic symptoms and even when infected or complicated by stones or neoplasms produces symptoms which are generally associated with much more common lesions, so that in the majority of cases it is only discovered during routine investigation. The symptoms of infection resulting from a stagnant pool of urine enclosed in a narrow-necked, atonic pouch need no description.

The disturbance of micturition does, however, require further thought. The difficulty of micturition, the residual urine and perhaps the grossly distended bladder, are often out of all proportion to the degree of bladder-neck obstruction, even in cases without severe infection. This is due to interference with the normal physiology of micturition, and lack of appreciation of this fact led to certain forms of treatment advocated by the earlier writers which we all now know to be useless. The voluntary initiation of the act of micturition is preceded by a sudden rise of intravesical pressure which fires off the detrusor reflex, which in turn causes the internal sphincter to open. Now, if there is a large atonic sac incapable of contraction, the sudden rise of bladder tension is absorbed in the flaccid pouch and the pressure required to fire off the detrusor reflex does not build up. The desire to micturate passes off and the bladder goes on filling slowly and may become palpable well above the pubes without causing much discomfort. The characteristic absence of overflow incontinence in these cases is also accounted for by the fact that the bladder may be very full, but the tension is low.

Similarly the fact, recorded by several writers, that the renal function is often very good in spite of a distended bladder, may be accounted for by the low resistance to urine entering the bladder from above, and this has led Hamilton (1943) to regard the diverticular blow-out as a safety-valve mechanism. This reflux into the diverticulum can often be demonstrated during cystography. Under the fluoroscopic screen the size of the pouch can be seen to increase considerably when the patient is instructed to try and pass urine against a closed sphincter. A proper understanding of this phenomenon effectively disposes of such methods of treatment as resecting the neck of the diverticulum so as to let it drain properly, and also explains why a suprapubic cystotomy is useless as a means of permanent relief, or even as a method of cleaning up the pouch prior to operation. It has to be washed out mechanically, it will not and cannot drain on its own.

*Hæmaturia* is always an anxious finding until its source is accurately localized. Carcinomatous diverticula are all too common for this hæmaturia to be considered lightly as due to prostatic bleeding or infection.

The classical symptom of "double micturition" referred to in all the books is a very rare phenomenon and Dees stated that it was not present in one of the 95 Brady Institute cases he reviewed. Even so, if there is much difficulty in washing a bladder clean before cystoscopy in a man of prostatic age, one should be suspicious and have a very good search for a diverticular orifice. Such openings can be very difficult to find in a prostatic bladder and a cystogram may be necessary for confirmation.

#### DIAGNOSIS

This is made by cystoscopy and cystography. We are all familiar with the introduction of opaque catheters into the diverticulum, with contrasting strengths of opaque medium, with air filling and oblique views, while the difficulty of finding the orifice cystoscopically has already been stressed, but I would refer to the diagnosis of what lies *inside* the cavity. Even

lapping the bulb with the gracilis muscle transplanted from the thigh. Thirdly I would refer to the operation introduced by our President, Mr. Terence Millin, in 1938, of surrounding the bulb with ribbon catgut. These last two procedures have had considerable success because they do produce a permanent fibrous constriction around the urethra. (I do not believe that the transplanted muscle can retain any contractility.) However the disadvantage of these operations where the bulbous urethra is completely surrounded, either by muscle, fascia or catgut, is that, whilst the encircling pressure is equally applied to the corpus spongiosum, it is unequally applied to the urethral mucosa, as the latter is not centrally situated within the corpus. Trophic ulceration of the mucosa, with fistula, and, later, stricture formation is liable to occur, particularly in those cases due to spina bifida.

The object of all these operations, including my present one, is the same: to produce an occlusive infolding of the urethral mucosa, supported by the vascular tissue of the corpus spongiosum with its natural elasticity. This is brought about by plication, not of the bulbo-cavernosus muscle, but of the corpus spongiosum itself by means of four or five silk sutures. The plication is carried out over a rubber catheter in the urethra. The size of the catheter should depend, to a certain extent, on the degree of incontinence. For the average case a 15 Ch Tiemann catheter is used. If the incontinence is greater then a catheter of lesser calibre is indicated. The catheter is left in situ for five days and then removed.

[A film demonstrating the operative technique was then shown. This was followed by a slide of a post-operative urethrogram showing the constriction produced in the bulb by the plication sutures.]

This is a minor surgical procedure. It can do no harm and in a large proportion of cases will help to alleviate this most distressing complaint.

[March 24, 1949]

## Vesical Diverticula. [Abridged]

By HOWARD G. HANLEY, M.D., F.R.C.S.

THE subject of vesical diverticula has not been discussed at this Section for many years. In 1935, Mr. Ogier Ward gave his Presidential Address on bladder diverticulum but, apart from several specimens shown at clinico-pathological meetings, we have to go back twenty-six years, to find the last time when the subject was debated (July 1923):

Compared with such subjects as lithiasis, stricture and hydronephrosis, diverticulum of the bladder is only a recently discovered disease, and although Pean in 1895 removed the first diverticulum from a 15-year-old girl, only 5 cases were recorded in the literature up to 1906. Since then there have been several outstanding papers on the subject and many series of cases have been recorded. The majority of the large series published have been collected from the various clinics in America and are the work of several surgeons, so that Mr. Ogier Ward's series of 53 cases published in 1938 is still one of the largest personal collections.

Unfortunately we have no agreed distinction between a very deep sacculation and a very small diverticulum, but in my own operation notes I have always recorded the depth to which a ureteric catheter would pass into the sac, and anything shallower than 2 cm. has been excluded from my 16 cases discussed here.

The comparatively recent recognition of the condition is not surprising when we remember that a diverticulum *per se* may cause no symptoms whatever, and has no specific syndrome, so that it is only the more modern diagnostic aids such as cystoscopy and X-rays which reveal the full extent of the pathology.

### ÆTIOLOGY

The ætiology of the large true diverticulum is still in doubt, but most people believe that even if there is a congenital weakness of the bladder wall, some obstructive factor must be added before the clinical "blow-out" occurs; relief of this obstruction forms an equally important, if not the most important part of treatment.

A few diverticula have been found in women, sometimes without any evidence of obstruction, but most are to be found in men with fibrous bladder-neck obstruction or benign prostatic obstruction of the fibrotic type rather than the large adenomatous variety.

operation and should be performed primarily whenever retention in the sac is demonstrated. Their best results were from diverticulectomy followed by resection, but a few prostatectomies were performed.

I personally reserve resection for fibrous bladder neck and carcinomatous cases with obstruction, so that I do not consider myself a resectionist. I have treated 2 fibrous prostate cases associated with diverticula by this means—without any benefit at all—both required a subsequent diverticulectomy. I note that Mr. Ogier Ward was no more successful in 4 cases where he employed resection, so that my impression is that few, if any, urologists in this country would expect endoscopic resection alone to prove sufficient in diverticula cases.

We now come to the symptomless diverticulum, either rendered so by relief of obstruction or discovered accidentally. This is rarely referred to in the books, but I believe that unless there are serious contra-indications, an effort should be made to remove all sizable pouches with narrow necks, even if they are not causing symptoms, because of the complications they seem to develop sooner or later. I have come to this conclusion because of my own 16 cases, 2 had stones and 2 contained growths—1 of which I did not detect or suspect until it had been made into a museum specimen. I feel sure that growths inside the diverticula are much more common than we imagine, and with this belief in mind I have looked through several of the more recent series of cases and find a significant percentage of growths recorded, several of which were unsuspected and only discovered during the diverticulectomy. This is a very serious argument against prostatic resection and leaving the sac in situ.

TABLE II

| Author                      | Date | No. of cases | No. of growths | % of growths | % of calculi |
|-----------------------------|------|--------------|----------------|--------------|--------------|
| Judd and Scholl .. ..       | 1924 | 133          | 4              | 3.0          | 9            |
| Kutzman .. ..               | 1933 | 72           | 0              | 0            | 0            |
| Ogier Ward .. ..            | 1938 | 53           | 4              | 7.5          | 22.6         |
| Dees .. ..                  | 1940 | 95           | 6              | 6.3          | 10.5         |
| Thompson, Cabot, Kermott .. | 1940 | 96           | 0              | 0            | 0            |
| Kimborough .. ..            | 1941 | 30           | 1              | 3.3          | 10.0         |
| Hamilton .. ..              | 1943 | 22           | 1              | 4.5          | 18           |
| Hellstrom .. ..             | 1945 | 20           | 3              | 15.0         | 20           |

Table II merely shows the percentage of neoplasms found in some of the more recent series of diverticula. I have included the percentage of calculi found because of the fact that the two series without any recorded neoplasms also contained no stones, so that these cases appear to be singularly free from the complications which beset other patients with like pathology.

Abeshouse, in presenting 4 new cases, reviews the literature up to 1943 but had collected only 95 primary carcinomas. To my mind this low figure is explained by the fact that surgeons do not write up one or two cases of an already reported condition. They wait until they have a series so that the twos and threes go unrecorded. For example Muellner (1946), in reporting a case which had not been diagnosed before operation, showed it at a clinical meeting in Boston, and, during the subsequent discussion, those present accounted for a further twelve carcinomata not reported in the literature.<sup>1</sup>

There are no specific symptoms of a growth in a diverticulum. Hæmaturia is probably common—but it is not uncommon in a simple diverticulum. Ogier Ward found hæmaturia in 18 of his 53 patients but only 4 of these had a neoplasm. In Abeshouse's review (1943) of 95 cases the diagnosis was made cystoscopically on 33 occasions. It was *not* made until the time of operation in 42 cases, while 18 growths were only discovered at autopsy.

A correct pre-operative diagnosis was only made in 33 of 54 cases in which cystoscopy was employed.

Muellner (1946) and Pearlman (1948) have both recorded cases where the growth was not detected before removal of the diverticulum. I have had two carcinomatous diverticula in 16 cases, one of which was unsuspected before operation; so that I will continue to remove all larger diverticula, even if symptomless, because I think they are potentially dangerous.

#### PROGNOSIS

When a carcinoma is associated with a diverticulum the prognosis is obviously very serious. The results of treatment in Abeshouse's collected review are very depressing. There were 61 radical operations with an operative mortality of 26%, while over 50% were dead within two years, and these were men between 50 and 65 years old, not nearly as old as the average prostatic patient. My own 2 cases were dead within four months and two years respectively; one from uræmia with local recurrence and the other from deposits, chiefly in his liver.

Although it is not suggested in the literature, I wonder whether we should not treat a

<sup>1</sup>In this present discussion 13 unrecorded cases were noted.

with the aid of a special cystoscopic beak and a 135 degrees telescope as used by Gorro (1946) to insert inside the orifice, we cannot be sure there is no growth inside it without exploring it digitally. Several excellent cystograms showing growths inside diverticula have been published by different authors, but many more have not been visualized, and a clear-cut diverticular outline is no guarantee that serious pathology can be excluded.

#### TREATMENT

Some of the views on treatment are diametrically opposed. We may safely say that any large sac which is unable to empty itself properly during micturition will require surgical treatment eventually, while any degree of urinary obstruction present must be relieved or the diverticulectomy will be a waste of time.

The relief of the obstruction, whether it be due to a small adenomatous prostate, a fibrous bladder neck or a urethral stricture, can be treated according to personal preference. Some surgeons, having relieved the obstruction, leave the diverticulum *in situ*, provided it is not too large and has not got too narrow a neck. The case can then be reviewed later to decide whether the diverticulum is causing symptoms or not. Others consider that the diverticulum and its infection should be removed before the prostate is attacked if both cannot be removed in one operation.

Some authors still advocate the resection of the narrow diverticular orifice so as to aid in its drainage. This is unsound physiology for it may be easier for the detrusor to force urine into the lax diverticulum than to raise the vesical pressure enough to start off the detrusor reflex, and so open the sphincter.

I once opened up the neck of a small 1 inch diverticulum during the operation of prostatectomy. Nearly two years later the patient returned complaining of difficulty of micturition. He had a diverticulum as large as a billiards ball and 6 oz. of residual urine in his bladder, in spite of the absence of any bladder-neck obstruction. All his symptoms were relieved by excision of this diverticulum—which was extremely difficult and convinced me that the correct time to perform a diverticulectomy is during the first operation. The order of procedure should be diverticulectomy followed by prostatectomy, never the reverse order. Incidentally I have found that retropubic prostatectomy is perfectly straightforward after a diverticulectomy.

If one employs perurethral resection for the relief of the obstruction, the situation is altered in that the bladder has not been opened and it matters little from the technical point of view whether the diverticulum is removed first or last.

With a clean bladder and a fit patient, a one-stage operation removing obstruction and sac together is the ideal procedure, thereby shortening the patient's convalescence. A one-stage operation, however, can be a very hazardous performance with an infected bladder, covered in hæmorrhagic exudate and phosphatic debris as they sometimes are, and I believe that the infection must always be controlled first. This is not always easy. I have had some success with Mr. Riches' irrigation apparatus using Suby's solution, but I have yet to find a satisfactory method of irrigating a large diverticulum itself if it has a narrow neck. All irrigation methods require a long period of catheter drainage which I do not like before prostatectomy, while a suprapubic cystotomy may clean up some of the bladder infection, but it will not help the diverticulum to drain.

While agreeing that a one-stage combined operation is the ideal, it so happens that I have only been able to do this when there was a fibrous neck type of obstruction, and these were treated by Irwin's clamp incisor which I have found most useful on such occasions. I have not, as yet, had a patient fit and clean enough to stand a prostatectomy and a diverticulectomy at the one sitting.

In 1940, Thompson and his colleagues reported 96 Mayo clinic cases treated solely by perurethral resection in the first instance. They say that it is easy to perform a diverticulectomy later if necessary, but they do not state how often they had to do this in their 96 patients. They considered that their results from resection were better than from prostatectomy, having a much shorter convalescence, and although they say that diverticulectomy was rarely performed during the years covered by their review (1932-37) they give a list of indications for diverticulectomy which includes: (a) Medium and large diverticula with tight orifices; (b) relatively young men where the diverticulum does not drain well after resection—even if symptoms are slight; (c) cases where the ureter is obstructed by the sac; and (d) complications such as calculi and neoplasms in the sac. They conclude, however, that resection alone will be sufficient for most cases. The criticism here is that if we perform a diverticulectomy according to their excellent list of indications we are left with small, clean, insignificant diverticula which we, too, might be tempted to leave alone after relieving the obstruction. Incidentally they encountered no case of stone or growth in their 96 cases, which is most unusual unless they were selected cases or very small diverticula.

Although Spence and Baird (1947) had previously performed a resection and waited to see how the diverticulum progressed, they now consider that diverticulectomy is a neglected

*In conclusion* here are some of the questions already raised.

What should be done with the symptomless diverticulum?

Should we attempt complete removal of the sac, or should we be satisfied with destruction of the mucosa?

If the sac and the obstruction cannot be removed together in one operation, should we remove the diverticulum first? Has a preliminary cystostomy any place?

What is the opinion concerning endoscopic resection?

Is it true that carcinoma in a diverticulum is commoner than we imagine, and is the prognosis of this complication as bad as it would seem from the literature?

#### BIBLIOGRAPHY

ABESHOUSE, B. S., and GOLDSTEIN, A. E. (1943) *J. Urol.*, 49, 534.

BADENOCH, A. W. (1949) *In press.*

BARNES, R. W. (1939) *J. Urol.*, 42, 794.

COUNCIL, W. A. (1941) *J. Urol.*, 45, 382.

DEES, J. E. (1940) *J. Urol.*, 44, 467.

FERRIER, P. A. (1948) *Calif. med. J.*, 68, 357.

GORRO, A. P. (1946) *Urol. Cut. Rev.*, 50, 19.

HAMILTON, A. J. C. (1943) *Edin. med. J.*, 50, 513.

HELLSTROM, J. (1945) *Nord. Med. Hygien.*, 27, 1921.

JOLY, J. SWIFT (1923) *Proc. R. Soc. Med.*, 16 (Sect. Urol., p. 55).

JUDD, E. S., and SCHOLL, A. J. (1924) *Surg. Gynec. Obstet.*, 38, 14.

KIMBOROUGH, J. (1941) *J. Urol.*, 45, 368.

KRETSCHMER, H. L. (1940) *Surg. Gynec. Obstet.*, 71, 491.

KUTZMAN, A. A. (1933) *Surg. Gynec. Obstet.*, 56, 790.

MUELLNER, S. R. (1946) *J. Urol.*, 56, 427.

PEARLMAN, C. K., and BOBBETT, R. M. (1948) *J. Urol.*, 59, 1127.

ROSELL, J. R. (1948) *Arch. Esp. Urol.*, 4, 242.

SPENCE, H. M., and BAIRD, S. S. (1947) *J. Urol.*, 58, 327.

THOMPSON, G. J., KERMOY, L. H., and CABOT, H. (1940) *Surg. Gynec. Obstet.*, 70, 115.

WARD, R. OGIER (1938) *Brit. J. Surg.*, 25, 898.

WINSBURY-WHITE, H. P. (1940) *Proc. R. Soc. Med.*, 34, 766.

YOUNG, HUGH H. (1940) *J. Urol.*, 44, 458.

**Mr. H. P. Winsbury-White:** In my records of cases which I have done in recent times there were 32 diverticulectomy cases in a consecutive series. These occurred in the course of operations upon 266 cases for the removal of bladder-neck obstruction of various kinds. This gives an incidence of just over 12% for diverticulum in obstructive states, and incidentally they show the need for cystoscopy as a preliminary to removing obstructions from the bladder neck. It is my practice to carry out this procedure as a first step in the operation session, for, if a diverticulum is left behind, it will create sepsis which will continue indefinitely, although the obstruction is removed. There is, of course, no danger from the shallow saccules so commonly present.

It is interesting to note the different conditions which cause an impediment to the outflow from the bladder. In these 32 cases the figures are as follows: 15 simple enlargement of the prostate; 8 pure fibrous obstruction; 8 prostatic calculi; 1 malignant prostate.

In the 15 cases of simple enlargement of the prostate besides the adenomatous change in the gland an element of fibrosis was generally present. Thus, throughout the whole series of obstructions fibrosis was a dominating feature. It is hardly necessary to add that this change is generally an outstanding one with prostatic calculi. With two exceptions, the diverticula were all in the lower half of the bladder, generally on the posterior wall or floor and in the last situation they were somewhere in the vicinity of a ureteric orifice. In none of these cases did a ureter open into a diverticulum.

In 4 of the cases the sac contained a calculus, and in 2 of them there was also a stone in the bladder. In 1 of the latter cases there were actually 6 diverticula present each containing a stone.

**Treatment.**—I carried out two forms of treatment with this series of cases: the sac was resected either intra- or extra-vesically; in some of the cases where the sacs were multiple both forms of treatment were followed. As a general rule when the sac was 2 in. or more in depth I preferred to do an extravesical resection.

The case with 6 diverticula, each of which contained a stone, showed a particularly interesting feature. Although an excellent cystoscopic view of the interior of the bladder was obtained pre-operatively, yet there was not the slightest sign of the presence of a diverticulum from this examination. The orifices of all the sacs were so constricted that they were not visible. There was no difficulty in this case in locating and excising all of the sacs with their stones intravesically; the patient made a good recovery. In another case there were 4 diverticula at the base of the bladder all of which were too large to resect intravesically and they had to be done by the external approach. It may be imagined that in such a case as

carcinomatous diverticulum by total cystectomy in the first place as if it were a carcinoma of the bladder or by radium if that is what we do for carcinoma of the bladder. A simple diverticulectomy appears to be as unsatisfactory as a partial cystectomy.

#### OPERATIVE TREATMENT

The removal of a large diverticulum from the depths of the pelvis—matted in adhesions and fixed to the ureters—can be a very formidable procedure. Few urologists have the chance of operating on, say, 50 diverticula in a lifetime, so that the development of a routine technique is almost impossible, particularly as each case differs from the next so considerably.

Familiarity gained in doing total cystectomy cases has helped me considerably with the more recent diverticulum operations. Really good exposure with a trans-rectus incision is a great help while the advent of tubarine has made spinal anaesthesia almost redundant.

A preliminary cystotomy as a means of clearing up the bladder and diverticular infection is of debatable value. Personally I have found it of no help in draining the sac, while it leads to a contracted bladder, thus making the subsequent operation more difficult.

Council (1941) has devised a rubber balloon on the end of a rubber catheter which he inserts inside the sac. When distended the balloon makes the outline of the sac very much easier to define and also acts as a retractor if it is held *in situ* by a purse string round the orifice. Personally I have found ribbon gauze packing very efficient for this purpose—and it is puncture proof!

There are various methods of dealing with the sac where it cannot be removed. Rosell (1948) marsupialized a huge pouch after closing its communication with the bladder proper, and the results as shown by X-ray are quite remarkable.

Barnes (1939) incised the bladder wall down to the stoma of the sac which he opened on its presenting anterior surface, thus laying the sac open. He then cauterized the mucosa, obliterated the stoma and drained both cavities to the surface separately. Ferrier (1948) has modified this slightly by irrigating the isolated sac with 10% silver nitrate solution, and continuing in gradually decreasing strengths for about twelve days. The patient died five years later from carcinoma of the bladder, but there was no cystoscopy or autopsy.

In the surgery of diverticulum the ureter, buried deep down in the pelvis and bound to the sac, can be very difficult to define. There are many recorded instances of deliberate ligature, but these are merely mentioned in order to condemn them. However, it may be necessary to divide the ureter and reimplant it into the bladder after removal of the diverticulum. Where the ureter opens into the sac Hugh Young has devised a Y plastic operation in which the piece of mucosa containing the orifice is swung into the bladder to form part of the new bladder wall. Young also prefers the intravesical approach to all diverticula. Where possible he sucks the mucosa inside out, and by circumcising the orifice delivers it into the bladder by blunt dissection. For small sacs this is ideal, but for large ones I think it is a very difficult manoeuvre, particularly when the stoma is near the ureteric orifice, and I have seen the ureter drawn into the bladder and damaged, in spite of having a ureteric catheter *in situ*.

Several authors mention epididymo-orchitis as a tiresome complication of diverticulectomy, and routine vasectomy is advised by both Dees (1940) and Kimborough (1941). I have never done a vasectomy in these cases until the prostatectomy stage but if vasectomy is to be done at all, it might as well be done as soon as possible.

Phlebitis and pyelonephritis are complications also reported but the incidence of the latter is probably much less in these days of chemotherapy, while the dangers of pelvic cellulitis should be much reduced.

TABLE III

| Cases | First operation                                      | Second operation       | Comments                   |
|-------|------------------------------------------------------|------------------------|----------------------------|
| 3     | Diverticulectomy                                     | Prostatectomy          | Two growths                |
| 1     | Diverticulectomy                                     | Retropubic             | Stone                      |
| 2     | Diverticulectomy                                     | Stricture              | Stone                      |
| 2     | Diverticulectomy                                     | Division of median bar | One stage                  |
| 2     | Cold punch                                           | Diverticulectomy       |                            |
| 1     | Prostatectomy                                        | Diverticulectomy       | Died 22 days               |
| 1     | Prostatectomy                                        | Operation refused      | Died 2 years               |
| 1     | Prostatectomy                                        | Widening of stoma      | Excised later              |
| 1     | Division of bar                                      | Mucosa removed         | One stage                  |
| 1     | Cystotomy, then prostatectomy, then diverticulectomy |                        | Suspect carcinoma prostate |
| 1     | Diverticulectomy (female)                            |                        | No obstruction             |

Each diverticulum has to be separately assessed, and no one form of operation or approach will suffice for every case. Table III is a list of my own cases showing what was done to each one. In addition to these cases, there were 5 smaller diverticula seen before prostatectomy and left alone, and 3 smallish diverticula associated with fibrous bladder-neck obstructions, also left alone. These cases were seen over a ten-year period, and, looking back on some of them, I do not think I would carry out the same procedures in all cases again.



*In conclusion* here are some of the questions already raised.

What should be done with the symptomless diverticulum?

Should we attempt complete removal of the sac, or should we be satisfied with destruction of the mucosa?

If the sac and the obstruction cannot be removed together in one operation, should we remove the diverticulum first? Has a preliminary cystotomy any place?

What is the opinion concerning endoscopic resection?

Is it true that carcinoma in a diverticulum is commoner than we imagine, and is the prognosis of this complication as bad as it would seem from the literature?

#### BIBLIOGRAPHY

- ABESHOUSE, B. S., and GOLDSTEIN, A. E. (1943) *J. Urol.*, 49, 534.  
 BADENOCH, A. W. (1949) In press.  
 BARNES, R. W. (1939) *J. Urol.*, 42, 794.  
 COUNCIL, W. A. (1941) *J. Urol.*, 45, 382.  
 DEES, J. E. (1940) *J. Urol.*, 44, 467.  
 FERRIER, P. A. (1948) *Calif. med. J.*, 68, 357.  
 GORRO, A. P. (1946) *Urol. Cut. Rev.*, 50, 19.  
 HAMILTON, A. J. C. (1943) *Edin. med. J.*, 50, 513.  
 HELLSTROM, J. (1945) *Nord. Med. Hygiea*, 27, 1921.  
 JOLY, J. SWIFT (1923) *Proc. R. Soc. Med.*, 16 (Sect. Urol., p. 55).  
 JUDD, E. S., and SCHOLL, A. J. (1924) *Surg. Gynec. Obstet.*, 38, 14.  
 KIMBOROUGH, J. (1941) *J. Urol.*, 45, 368.  
 KRETSCHMER, H. L. (1940) *Surg. Gynec. Obstet.*, 71, 491.  
 KUTZMAN, A. A. (1933) *Surg. Gynec. Obstet.*, 56, 790.  
 MUELLNER, S. R. (1946) *J. Urol.*, 56, 427.  
 PEARLMAN, C. K., and BOBBETT, R. M. (1948) *J. Urol.*, 59, 1127.  
 ROSELL, J. R. (1948) *Arch. Esp. Urol.*, 4, 242.  
 SPENCE, H. M., and BAIRD, S. S. (1947) *J. Urol.*, 58, 327.  
 THOMPSON, G. J., KERMOTT, L. H., and CABOT, H. (1940) *Surg. Gynec. Obstet.*, 70, 115.  
 WARD, R. OGIER (1938) *Brit. J. Surg.*, 25, 898.  
 WINSBURY-WHITE, H. P. (1940) *Proc. R. Soc. Med.*, 34, 766.  
 YOUNG, HUGH H. (1940) *J. Urol.*, 44, 458.

**Mr. H. P. Winsbury-White:** In my records of cases which I have done in recent times there were 32 diverticulectomy cases in a consecutive series. These occurred in the course of operations upon 266 cases for the removal of bladder-neck obstruction of various kinds. This gives an incidence of just over 12% for diverticulum in obstructive states, and incidentally they show the need for cystoscopy as a preliminary to removing obstructions from the bladder neck. It is my practice to carry out this procedure as a first step in the operation session, for, if a diverticulum is left behind, it will create sepsis which will continue indefinitely, although the obstruction is removed. There is, of course, no danger from the shallow saccules so commonly present.

It is interesting to note the different conditions which cause an impediment to the outflow from the bladder. In these 32 cases the figures are as follows: 15 simple enlargement of the prostate; 8 pure fibrous obstruction; 8 prostatic calculi; 1 malignant prostate.

In the 15 cases of simple enlargement of the prostate besides the adenomatous change in the gland an element of fibrosis was generally present. Thus, throughout the whole series of obstructions fibrosis was a dominating feature. It is hardly necessary to add that this change is generally an outstanding one with prostatic calculi. With two exceptions, the diverticula were all in the lower half of the bladder, generally on the posterior wall or floor and in the last situation they were somewhere in the vicinity of a ureteric orifice. In none of these cases did a ureter open into a diverticulum.

In 4 of the cases the sac contained a calculus, and in 2 of them there was also a stone in the bladder. In 1 of the latter cases there were actually 6 diverticula present each containing a stone.

*Treatment.*—I carried out two forms of treatment with this series of cases: the sac was resected either intra- or extra-vesically; in some of the cases where the sacs were multiple both forms of treatment were followed. As a general rule when the sac was 2 in. or more in depth I preferred to do an extravesical resection.

The case with 6 diverticula, each of which contained a stone, showed a particularly interesting feature. Although an excellent cystoscopic view of the interior of the bladder was obtained pre-operatively, yet there was not the slightest sign of the presence of a diverticulum from this examination. The orifices of all the sacs were so constricted that they were not visible. There was no difficulty in this case in locating and excising all of the sacs with their stones intravesically; the patient made a good recovery. In another case there were 4 diverticula at the base of the bladder all of which were too large to resect intravesically and they had to be done by the external approach. It may be imagined that in such a case as

this, the amount of mobilization necessary at the base of the bladder was considerable, therefore the patient suffered a good deal of shock, nevertheless he made a good recovery from the operation.

In reviewing the 32 cases as a whole it transpires that 17 were extravesical resections, and 18 intravesical resections (35 operations): the mortality for these diverticulectomies was a total of 3 cases, which works out at 9.3%.

*Technique of operation.*—With either approach I would pack the diverticulum fairly tightly with ribbon gauze. On the extravesical approach, this made the sac easily palpable, and after its neck was severed from the bladder the remaining orifice in the latter was firmly stitched with interrupted catgut sutures. I was then careful to stitch a wide, corrugated rubber drain to the suture line extravesically. In the convalescence I was never in a hurry to remove this, always being certain that the temperature was settled before I attempted to shorten the drain.

For the intravesical approach, after gripping the margin in two places with Aliss's forceps, a circular incision was made round the orifice of the sac and then dissection proceeded. The important part about this operation is to make no attempt to close the resulting extravesical cavity, it must be left draining freely into the bladder. The after-course was usually eminently satisfactory.

The question as to when the sac should be removed in relation to the removal of the bladder-neck obstruction has always been a perplexing one, but my figures are as follows:

In 11 cases the sac and the bladder-neck obstruction were removed in one stage, i.e. at the same operation. There was no death from this series. In 17 cases the diverticulum was removed at the first stage of a two-stage procedure, that is to say the bladder-neck obstruction was removed at the second operation. There were 2 deaths in this series. 4 were done at the second stage of a two-stage procedure, that is to say the bladder was merely drained at the first stage and at the second both the diverticulum and bladder-neck obstruction were removed. I had 1 death from this series.

Mr. E. W. Riches considered that the removal of the diverticulum and the prostate by a single-stage operation was the ideal and was possible in many cases. If circumstances made a two-stage operation necessary the diverticulum should be removed first and the bladder drained, unless the prostate was suitable for endoscopic resection when this could be done as the first stage. The secondary removal of a diverticulum some time after prostatectomy could be a difficult procedure; he showed a slide of one case where this had been necessary owing to persistence of infection and a fistula. The main advantage of cystoscopy before prostatectomy was the discovery of a diverticulum; any large sac should be removed or persistent sepsis must be expected. It was always an advantage to pass a catheter into the ureter before diverticulectomy and leave it in position during the operation.

He had seen 2 cases of malignant and 1 of benign growth in a diverticulum; malignant growths soon became inoperable because of fixation to the pelvic wall.

Mr. Ogier Ward said that he wished particularly to support Mr. Hanley in his statements concerning treatment. If a diverticulum were sufficiently important to require operative treatment then in almost every case it was necessary, not only to excise the sac, but also to treat the obstruction, at whatever site it existed, which had given rise to back pressure. As the sac has no contractile power, the operation of incising the orifice in the hope that this would give drainage was in his opinion a useless procedure. In most cases he performed diverticulectomy by cutting around the orifice through the opened bladder and drawing the sac into the bladder as it was freed by dissection; in a few instances he made a lateral incision in the bladder wall and continued this around the orifice of the sac.

If, as was so often the case, the obstructive factor was stenosis of the col vesicæ he usually treated this by perurethral resection about two weeks after the diverticulectomy.

Mr. J. H. Carver raised the question of dealing with retro-trigonal diverticula and wondered if any members of the Section had experience of the transperitoneal approach recommended by Puigvert of Barcelona.

Mr. L. N. Pyrah: The best operation for diverticulum of the bladder is an extravesical removal of the diverticulum and this is normally possible for large and medium-sized diverticula. In the days before infection could be largely controlled by the use of the sulphonamides and penicillin, the recovery of the patient following the removal of a suppurating diverticulum of the bladder by the transvesical method was not infrequently jeopardized because of wound infection; necrotic extravesical fat and free discharge of pus were not uncommon. If, on the other hand, the diverticulum is removed without opening the bladder, the wound will heal by first intention.

The operation is done with the bladder moderately distended with saline. A long suprapubic incision is made separating the recti. The bladder is mobilised by stripping the peritoneum from the superior and posterior surfaces of the bladder and from the diverticulum; the latter can be recognized by the existence of a sulcus between it and the bladder. The diverticulum is often very adherent to the lateral pelvic wall but it can be gradually raised out of the pelvis and its deeper aspect exposed. The ureter must be identified and dissected from the wall of the diverticulum. The diverticulum is attached by dense adhesions to the bladder over a wide surface, far wider, in fact, than the size of the opening of the diverticulum would indicate; these adherent surfaces must be dissected apart until the diverticulum is connected to the bladder only by its neck. The diverticulum having been delivered completely out of the wound, the fibrous tissue round the neck is carefully divided until it is attached to the bladder by a narrow tube of mucous membrane. The mucosa is gently crushed with a crushing clamp and ligatured in two places, and the diverticulum cut away between the ligatures. The muscle of the bladder wall is drawn over the ligatured stump of the diverticulum by a number of interrupted catgut stitches or by a purse-string suture, just as an appendix stump is buried in the wall of the cecum; a second layer of interrupted or continuous catgut stitches completes the operation. The abdominal wound is closed, leaving a small drainage tube down to the site of the diverticulum. An indwelling catheter is retained in the urethra for ten days.

Mr. Ashton Miller: I first came across the operation Mr. Pyrah has just described in a Hungarian journal (*Acta Urol.*, 1948, 2, 15). It is essential that the neck of the diverticulum be displayed by dividing the thickened pelvic fascia covering both diverticulum and bladder before the purse-string suture is inserted.

Mr. A. Wilfrid Adams said that it was important to remember the frequent multiplicity of diverticula and that symptoms from continued infection might persist as long as one pouch remained. Complete removal was formidable and had sometimes required two surgical attacks.

His own efforts at diverticulectomy extravesically had involved tough dissection with obvious hazards. Discovering a pus-laden sac recently during combined herniotomy and prostatectomy in a poor subject, he tried the alternative approach via the bladder interior. The mucosal lining of the pouch was seized with forceps, readily drawn into the bladder, amputated, and the muscle margin stitched together with curative results. This method was handy where the bladder was already open. However, Mr. Pyrah had so far converted him that in ordinary cases he will resume the extravesical approach. He was strengthened in this opinion after hearing the amplifying remarks of Mr. Ashton Miller pointing out that the sac was dissected submucosally after incision around the neck of the tough fibrous coat. Evidently this affords an easy line of cleavage.

What was to be done when there was concomitant obvious prostatic obstruction calling for active treatment?

In his view the coincidental discovery of diverticula may not call for their removal. The prostate, not the pouch, should receive priority of treatment. This was especially so if the patient was not a favourable subject and the diverticula, though roomy, appeared clean and did not jeopardize the kidney by pressing on the adjacent ureter.

The patient's great relief from his prostatism might well satisfy him. If trouble did persist, subsequent diverticulectomy was safer and surer, especially after a trans-urethral operation with a scar-free abdomen.

Mr. H. K. Vernon: *Case of bladder diverticulum containing massive stone.*—Male, aged 62 years, admitted with slight rectal bleeding but denied he had any urinary symptoms except frequency twice at night. X-ray and-cystoscopy revealed a massive stone inside a diverticulum and a smaller vesical calculus.

*Operations.*—21.2.49: Removal of vesical calculus and diverticulum complete with stone transvesically. Right ureter opened into diverticulum and had to be divided and re-implanted into bladder. The stone and diverticulum were actually impacted in the pelvis and had to be removed with midwifery forceps.

23.3.49: Transurethral resection of bladder neck.

1.4.49: Suprapubic wound healed.

*Comment.*—This case illustrates how even a large diverticulum can be removed by the transvesical method of circumcising the orifice and dissecting out the sac.

JULY—UROL. 4

this, the amount of mobilization necessary at the base of the bladder was considerable, therefore the patient suffered a good deal of shock, nevertheless he made a good recovery from the operation.

In reviewing the 32 cases as a whole it transpires that 17 were extravesical resections, and 18 intravesical resections (35 operations): the mortality for these diverticulectomies was a total of 3 cases, which works out at 9.3%.

*Technique of operation.*—With either approach I would pack the diverticulum fairly tightly with ribbon gauze. On the extravesical approach, this made the sac easily palpable, and after its neck was severed from the bladder the remaining orifice in the latter was firmly stitched with interrupted catgut sutures. I was then careful to stitch a wide, corrugated rubber drain to the suture line extravesically. In the convalescence I was never in a hurry to remove this, always being certain that the temperature was settled before I attempted to shorten the drain.

For the intravesical approach, after gripping the margin in two places with Aliss's forceps, a circular incision was made round the orifice of the sac and then dissection proceeded. The important part about this operation is to make no attempt to close the resulting extravesical cavity, it must be left draining freely into the bladder. The after-course was usually eminently satisfactory.

The question as to when the sac should be removed in relation to the removal of the bladder-neck obstruction has always been a perplexing one, but my figures are as follows:

In 11 cases the sac and the bladder-neck obstruction were removed in one stage, i.e. at the same operation. There was no death from this series. In 17 cases the diverticulum was removed at the first stage of a two-stage procedure, that is to say the bladder-neck obstruction was removed at the second operation. There were 2 deaths in this series. 4 were done at the second stage of a two-stage procedure, that is to say the bladder was merely drained at the first stage and at the second both the diverticulum and bladder-neck obstruction were removed. I had 1 death from this series.

Mr. E. W. Riches considered that the removal of the diverticulum and the prostate by a single-stage operation was the ideal and was possible in many cases. If circumstances made a two-stage operation necessary the diverticulum should be removed first and the bladder drained, unless the prostate was suitable for endoscopic resection when this could be done as the first stage. The secondary removal of a diverticulum some time after prostatectomy could be a difficult procedure; he showed a slide of one case where this had been necessary owing to persistence of infection and a fistula. The main advantage of cystoscopy before prostatectomy was the discovery of a diverticulum; any large sac should be removed or persistent sepsis must be expected. It was always an advantage to pass a catheter into the ureter before diverticulectomy and leave it in position during the operation.

He had seen 2 cases of malignant and 1 of benign growth in a diverticulum; malignant growths soon became inoperable because of fixation to the pelvic wall.

Mr. Ogier Ward said that he wished particularly to support Mr. Hanley in his statements concerning treatment. If a diverticulum were sufficiently important to require operative treatment then in almost every case it was necessary, not only to excise the sac, but also to treat the obstruction, at whatever site it existed, which had given rise to back pressure. As the sac has no contractile power, the operation of incising the orifice in the hope that this would give drainage was in his opinion a useless procedure. In most cases he performed diverticulectomy by cutting around the orifice through the opened bladder and drawing the sac into the bladder as it was freed by dissection; in a few instances he made a lateral incision in the bladder wall and continued this around the orifice of the sac.

If, as was so often the case, the obstructive factor was stenosis of the col vesicæ he usually treated this by perurethral resection about two weeks after the diverticulectomy.

Mr. J. H. Carver raised the question of dealing with retro-trigonal diverticula and wondered if any members of the Section had experience of the transperitoneal approach recommended by Puigvert of Barcelona.

Mr. L. N. Pyrah: The best operation for diverticulum of the bladder is an extravesical removal of the diverticulum and this is normally possible for large and medium-sized diverticula. In the days before infection could be largely controlled by the use of the sulphonamides and penicillin, the recovery of the patient following the removal of a suppurating diverticulum of the bladder by the transvesical method was not infrequently jeopardized because of wound infection; necrotic extravesical fat and free discharge of pus were not uncommon. If, on the other hand, the diverticulum is removed without opening the bladder, the wound will heal by first intention.

The operation is done with the bladder moderately distended with saline. A long suprapubic incision is made separating the recti. The bladder is mobilised by stripping the peritoneum from the superior and posterior surfaces of the bladder and from the diverticulum; the latter can be recognized by the existence of a sulcus between it and the bladder. The diverticulum is often very adherent to the lateral pelvic wall but it can be gradually raised out of the pelvis and its deeper aspect exposed. The ureter must be identified and dissected from the wall of the diverticulum. The diverticulum is attached by dense adhesions to the bladder over a wide surface, far wider, in fact, than the size of the opening of the diverticulum would indicate; these adherent surfaces must be dissected apart until the diverticulum is connected to the bladder only by its neck. The diverticulum having been delivered completely out of the wound, the fibrous tissue round the neck is carefully divided until it is attached to the bladder by a narrow tube of mucous membrane. The mucosa is gently crushed with a crushing clamp and ligatured in two places, and the diverticulum cut away between the ligatures. The muscle of the bladder wall is drawn over the ligatured stump of the diverticulum by a number of interrupted catgut stitches or by a purse-string suture, just as an appendix stump is buried in the wall of the cæcum; a second layer of interrupted or continuous catgut stitches completes the operation. The abdominal wound is closed, leaving a small drainage tube down to the site of the diverticulum. An indwelling catheter is retained in the urethra for ten days.

**Mr. Ashton Miller:** I first came across the operation Mr. Pyrah has just described in a Hungarian journal (*Acta Urol.*, 1948, 2, 15). It is essential that the neck of the diverticulum be displayed by dividing the thickened pelvic fascia covering both diverticulum and bladder before the purse-string suture is inserted.

**Mr. A. Wilfrid Adams** said that it was important to remember the *frequent multiplicity of diverticula* and that symptoms from continued infection might persist as long as one pouch remained. Complete removal was formidable and had sometimes required two surgical attacks.

His own efforts at diverticulectomy extravesically had involved tough dissection with obvious hazards. Discovering a pus-laden sac recently during combined herniotomy and prostatectomy in a poor subject, he tried the alternative approach via the bladder interior. The mucosal lining of the pouch was seized with forceps, readily drawn into the bladder, amputated, and the muscle margin stitched together with curative results. This method was handy where the bladder was already open. However, Mr. Pyrah had so far converted him that in ordinary cases he will resume the extravesical approach. He was strengthened in this opinion after hearing the amplifying remarks of Mr. Ashton Miller pointing out that the sac was dissected submucosally after incision around the neck of the tough fibrous coat. Evidently this affords an easy line of cleavage.

What was to be done when there was *concomitant obvious prostatic obstruction* calling for active treatment?

In his view the coincidental discovery of diverticula may not call for their removal. The prostate, not the pouch, should receive priority of treatment. This was especially so if the patient was not a favourable subject and the diverticula, though roomy, appeared clean and did not jeopardize the kidney by pressing on the adjacent ureter.

The patient's great relief from his prostatism might well satisfy him. If trouble did persist, subsequent diverticulectomy was safer and surer, especially after a trans-urethral operation with a scar-free abdomen.

**Mr. H. K. Vernon:** *Case of bladder diverticulum containing massive stone.*—Male, aged 62 years, admitted with slight rectal bleeding but denied he had any urinary symptoms except frequency twice at night. X-ray and cystoscopy revealed a massive stone inside a diverticulum and a smaller vesical calculus.

**Operations.**—21.2.49: Removal of vesical calculus and diverticulum complete with stone transvesically. Right ureter opened into diverticulum and had to be divided and re-implanted into bladder. The stone and diverticulum were actually impacted in the pelvis and had to be removed with midwifery forceps.

23.3.49: Transurethral resection of bladder neck.

1.4.49: Suprapubic wound healed.

**Comment.**—This case illustrates how even a large diverticulum can be removed by the transvesical method of circumcising the orifice and dissecting out the sac.

JULY—UROL. 4

this, the amount of mobilization necessary at the base of the bladder was considerable, therefore the patient suffered a good deal of shock, nevertheless he made a good recovery from the operation.

In reviewing the 32 cases as a whole it transpires that 17 were extravesical resections, and 18 intravesical resections (35 operations): the mortality for these diverticulectomies was a total of 3 cases, which works out at 9.3%.

*Technique of operation.*—With either approach I would pack the diverticulum fairly tightly with ribbon gauze. On the extravesical approach, this made the sac easily palpable, and after its neck was severed from the bladder the remaining orifice in the latter was firmly stitched with interrupted catgut sutures. I was then careful to stitch a wide, corrugated rubber drain to the suture line extravesically. In the convalescence I was never in a hurry to remove this, always being certain that the temperature was settled before I attempted to shorten the drain.

For the intravesical approach, after gripping the margin in two places with Allis's forceps, a circular incision was made round the orifice of the sac and then dissection proceeded. The important part about this operation is to make no attempt to close the resulting extravesical cavity, it must be left draining freely into the bladder. The after-course was usually eminently satisfactory.

The question as to when the sac should be removed in relation to the removal of the bladder-neck obstruction has always been a perplexing one, but my figures are as follows:

In 11 cases the sac and the bladder-neck obstruction were removed in one stage, i.e. at the same operation. There was no death from this series. In 17 cases the diverticulum was removed at the first stage of a two-stage procedure, that is to say the bladder-neck obstruction was removed at the second operation. There were 2 deaths in this series. 4 were done at the second stage of a two-stage procedure, that is to say the bladder was merely drained at the first stage and at the second both the diverticulum and bladder-neck obstruction were removed. I had 1 death from this series.

Mr. E. W. Riches considered that the removal of the diverticulum and the prostate by a single-stage operation was the ideal and was possible in many cases. If circumstances made a two-stage operation necessary the diverticulum should be removed first and the bladder drained, unless the prostate was suitable for endoscopic resection when this could be done as the first stage. The secondary removal of a diverticulum some time after prostatectomy could be a difficult procedure; he showed a slide of one case where this had been necessary owing to persistence of infection and a fistula. The main advantage of cystoscopy before prostatectomy was the discovery of a diverticulum; any large sac should be removed or persistent sepsis must be expected. It was always an advantage to pass a catheter into the ureter before diverticulectomy and leave it in position during the operation.

He had seen 2 cases of malignant and 1 of benign growth in a diverticulum; malignant growths soon became inoperable because of fixation to the pelvic wall.

Mr. Ogier Ward said that he wished particularly to support Mr. Hanley in his statements concerning treatment. If a diverticulum were sufficiently important to require operative treatment then in almost every case it was necessary, not only to excise the sac, but also to treat the obstruction, at whatever site it existed, which had given rise to back pressure. As the sac has no contractile power, the operation of incising the orifice in the hope that this would give drainage was in his opinion a useless procedure. In most cases he performed diverticulectomy by cutting around the orifice through the opened bladder and drawing the sac into the bladder as it was freed by dissection; in a few instances he made a lateral incision in the bladder wall and continued this around the orifice of the sac.

If, as was so often the case, the obstructive factor was stenosis of the col vesicæ he usually treated this by perurethral resection about two weeks after the diverticulectomy.

Mr. J. H. Carver raised the question of dealing with retro-trigonal diverticula and wondered if any members of the Section had experience of the transperitoneal approach recommended by Puigvert of Barcelona.

Mr. L. N. Pyrah: The best operation for diverticulum of the bladder is an extravesical removal of the diverticulum and this is normally possible for large and medium-sized diverticula. In the days before infection could be largely controlled by the use of the sulphonamides and penicillin, the recovery of the patient following the removal of a suppurating diverticulum of the bladder by the transvesical method was not infrequently jeopardized because of wound infection; necrotic extravesical fat and free discharge of pus were not uncommon. If, on the other hand, the diverticulum is removed without opening the bladder, the wound will heal by first intention.

The operation is done with the bladder moderately distended with saline. A long suprapubic incision is made separating the recti. The bladder is mobilised by stripping the peritoneum from the superior and posterior surfaces of the bladder and from the diverticulum; the latter can be recognized by the existence of a sulcus between it and the bladder. The diverticulum is often very adherent to the lateral pelvic wall but it can be gradually raised out of the pelvis and its deeper aspect exposed. The ureter must be identified and dissected from the wall of the diverticulum. The diverticulum is attached by dense adhesions to the bladder over a wide surface, far wider, in fact, than the size of the opening of the diverticulum would indicate; these adherent surfaces must be dissected apart until the diverticulum is connected to the bladder only by its neck. The diverticulum having been delivered completely out of the wound, the fibrous tissue round the neck is carefully divided until it is attached to the bladder by a narrow tube of mucous membrane. The mucosa is gently crushed with a crushing clamp and ligatured in two places, and the diverticulum cut away between the ligatures. The muscle of the bladder wall is drawn over the ligatured stump of the diverticulum by a number of interrupted catgut stitches or by a purse-string suture, just as an appendix stump is buried in the wall of the cæcum; a second layer of interrupted or continuous catgut stitches completes the operation. The abdominal wound is closed, leaving a small drainage tube down to the site of the diverticulum. An indwelling catheter is retained in the urethra for ten days.

**Mr. Ashton Miller:** I first came across the operation Mr. Pyrah has just described in a Hungarian journal (*Acta Urol.*, 1948, 2, 15). It is essential that the neck of the diverticulum be displayed by dividing the thickened pelvic fascia covering both diverticulum and bladder before the purse-string suture is inserted.

**Mr. A. Wilfrid Adams** said that it was important to remember the *frequent multiplicity of diverticula* and that symptoms from continued infection might persist as long as one pouch remained. Complete removal was formidable and had sometimes required two surgical attacks.

His own efforts at diverticulectomy extravesically had involved tough dissection with obvious hazards. Discovering a pus-laden sac recently during combined herniotomy and prostatectomy in a poor subject, he tried the alternative approach via the bladder interior. The mucosal lining of the pouch was seized with forceps, readily drawn into the bladder, amputated, and the muscle margin stitched together with curative results. This method was handy where the bladder was already open. However, Mr. Pyrah had so far converted him that in ordinary cases he will resume the extravesical approach. He was strengthened in this opinion after hearing the amplifying remarks of Mr. Ashton Miller pointing out that the sac was dissected submucosally after incision around the neck of the tough fibrous coat. Evidently this affords an easy line of cleavage.

What was to be done when there was *concomitant obvious prostatic obstruction* calling for active treatment?

In his view the coincidental discovery of diverticula may not call for their removal. The prostate, not the pouch, should receive priority of treatment. This was especially so if the patient was not a favourable subject and the diverticula, though roomy, appeared clean and did not jeopardize the kidney by pressing on the adjacent ureter.

The patient's great relief from his prostatism might well satisfy him. If trouble did persist, subsequent diverticulectomy was safer and surer, especially after a trans-urethral operation with a scar-free abdomen.

**Mr. H. K. Vernon:** *Case of bladder diverticulum containing massive stone.*—Male, aged 62 years, admitted with slight rectal bleeding but denied he had any urinary symptoms except frequency twice at night. X-ray and cystoscopy revealed a massive stone inside a diverticulum and a smaller vesical calculus.

**Operations.**—21.2.49: Removal of vesical calculus and diverticulum complete with stone transvesically. Right ureter opened into diverticulum and had to be divided and re-implanted into bladder. The stone and diverticulum were actually impacted in the pelvis and had to be removed with midwifery forceps.

23.3.49: Transurethral resection of bladder neck.

1.4.49: Suprapubic wound healed.

**Comment.**—This case illustrates how even a large diverticulum can be removed by the transvesical method of circumcising the orifice and dissecting out the sac.

JULY—UROL. 4



FIG. 1.

FIG. 1.—X-ray showing large stone inside diverticulum and small vesical calculus.



FIG. 2.

FIG. 2.—Photograph showing delivery of stone at operation by axis traction forceps.

(Photograph by W. W. Davey)

Figs. 1 and 2 are Mr. H. K. Vernon's case (see page 25).

#### *Case of Massive Stone in Bladder Diverticulum*

Mr. Clifford Morson said it was with some diffidence that he entered into competition with Mr. Vernon in describing a bizarre technique for the removal of a stone from a bladder diverticulum. Whereas Mr. Vernon must have borrowed his tools from an obstetrician, Mr. Morson had obtained his from the Orthopaedic Department.

In this case the stone weighed 2 lb. 2 oz., and was wedged in the bony pelvis. It could not have been removed with traction forceps without damaging the internal iliac vessels. The excitement when Mr. Vernon delivered the whole calculus from the pouch must have been intense, but his technique was equally effective. It consisted in the production of multiple fractures in the stone with a hammer and chisel, and its removal piecemeal.

The appearance of the X-ray picture resembled the head of a full-term foetus *in utero*. The picture and the fragments of stone were presented to the museum of the Royal College of Surgeons.

The President (Mr. Terence Millin), in summing up, said that Mr. Hanley had emphasized one point, perhaps but little appreciated, namely the high incidence of malignancy within these vesical pouches. Mr. Millin had personally seen 7 cases of such malignancy within the past two years. For this reason he preferred the extravasical type of operation. He endorsed most whole-heartedly the operation described by Mr. Pyrah and, in fact, used it almost exclusively. Where the bladder-neck obstruction was of the median bar type he employed a transurethral resection; where an adenomatous prostate was associated, he carried out a retropubic enucleation, usually at the same time as the diverticulectomy. In certain cases where an adenomatous prostate required intervention and where a relatively small diverticulum was present, he carried out a retropubic enucleation, leaving the diverticulum. If later increase in the size of the pouch or persistent infection seemed to demand a diverticulectomy this could be readily carried out without the well-known disadvantage of such an operation following a transvesical prostatectomy.

[April 28, 1949]

The following cases and specimens were shown:

(1) Bilateral Testicular New Growths. Implantation of Artificial Testes. (2) Innocent Papilloma of the Ureter.—Mr. J. H. CARVER.

Monorchism.—Mr. J. D. FERGUSSON.

(1) Total Prostatovesiculectomy. (2) Vesical Papillomatosis with Spread up the Ureter.—Mr. TERENCE MILLIN.

Megalo-ureter.—Mr. G. J. GRIFFITHS (introduced by Mr. TERENCE MILLIN).

Pedunculated Vascular Tumour of the Ureter.—Mr. WALTER GALBRAITH.

Carcinoma of Ureter.—Mr. STEPHEN POWER.

Bilateral Renal Calculi. Problem for Treatment.—Mr. H. J. MCCURRICH (introduced by Mr. TERENCE MILLIN).

(1) Glands in Nephro-ureterectomy for Tubercle (Child). (2) Inclusion of Intravenous Extension in Removal of Hypernephroma.—Mr. WILFRID ADAMS.

Anaplastic Carcinoma in Calculous Hydronephrosis.—Mr. J. GABE.



## Section of Pædiatrics

President—Professor J. M. SMELLIE, O.B.E., M.D., F.R.C.P.

[October 22, 1948, concluded]

**Polyostotic Fibrous Dysplasia.**—J. R. D. WEBB, O.B.E., M.R.C.P., D.P.H., D.C.H.

Boy, aged 5 years, was first seen in June 1948 with a history of a vague ache in the right hip and difficulty in walking. Child quite well otherwise. Has five brothers and sisters who are normal.

*On examination.*—Bony swelling in region of left frontal bone with orbit displaced downwards (fig. 1). Lower end of left ulna absent (fig. 5). While in hospital ran a mild pyrexia.

Chest normal. I.V.P. normal.

*Investigations.*—Serum phosphorus 4.6 mg.%; serum calcium 9 mg.%; acid phosphatase 2.5 units; alkaline phosphatase 6 units; Hb. 87%; R.B.C. 4,610,000; W.B.C. 5,200; E.S.R. 12 mm./hr.; sternal puncture 61.9% lymphos. Other cells normal. Wassermann reaction negative. Kahn test negative.

*Ophthalmic report.*—N.A.D.

*Radiological report* (figs. 2, 3, 4 and 5).—The features of X-rays are: (1) Broadening or expansion of bone. (2) Thinning of the cortex. (3) Characteristic rarefied and trabeculated appearance suggesting cystic disease. (4) Secondary deformities of affected bones. The commonest error in X-ray interpretation is to call these cases "cystic disease of the bones". The peculiar appearance of the lesions is due to replacement of the spongy bone and filling of the medullary cavity by fibrous tissue containing spicules of poorly calcified primitive bone.

*Report on biopsy from frontal bone.*—Microscopical section was shown at the meeting which demonstrated the features as described by Lichtenstein.

In 1938 Lichtenstein and Jaffe described 8 cases, and suggested the use of the term "polyostotic fibrous dysplasia" rather than the variety of titles which have been formerly used (see *Arch. Surg.*, 36, 874).

Lichtenstein summarized the condition as follows: (1) It is a skeletal developmental anomaly. (2) It usually affects several or many bones. (3) Often unilateral, yet lesions of the opposite side of the body do occur—in severe cases. (4) It is not an uncommon disease and appears in childhood and in young adolescents, usually females. (5) The cause is unknown although a congenital disorder is suggested, because of its dating back to childhood with slow evolution. (6) Unlike other anomalous skeletal developmental conditions such as multiple exostoses and achondroplasia, there is no familial incidence or hereditary tendency. (7) The femur and tibia are most commonly affected, yet the arm bones, skull, ribs, pelvis and phalanges may be affected. (8) The condition runs a slow progressive course over many years and there is a tendency to spontaneous fractures and a deformity of affected bones. (9) The chief pathological feature is a disturbed function or development of the bone-forming mesenchyme and it results in the filling of the medullary cavity of the affected bones by fibrous tissues, in which spicules of poorly calcified primitive fibre bone are developed by osseous metaplasia. Some areas show collagenous differentiation with little new bone



FIG. 1.

FIG. 1.—X-ray showing large stone inside diverticulum and small vesical calculus.



FIG. 2.

FIG. 2.—Photograph showing delivery of stone at operation by axis traction forceps.

(Photograph by W. W. Davey)

Figs. 1 and 2 are Mr. H. K. Vernon's case (see page 25).

### *Case of Massive Stone in Bladder Diverticulum*

Mr. Clifford Morson said it was with some diffidence that he entered into competition with Mr. Vernon in describing a bizarre technique for the removal of a stone from a bladder diverticulum. Whereas Mr. Vernon must have borrowed his tools from an obstetrician, Mr. Morson had obtained his from the Orthopaedic Department.

In this case the stone weighed 2 lb. 2 oz., and was wedged in the bony pelvis. It could not have been removed with traction forceps without damaging the internal iliac vessels. The excitement when Mr. Vernon delivered the whole calculus from the pouch must have been intense, but his technique was equally effective. It consisted in the production of multiple fractures in the stone with a hammer and chisel, and its removal piecemeal.

The appearance of the X-ray picture resembled the head of a full-term *fœtus in utero*. The picture and the fragments of stone were presented to the museum of the Royal College of Surgeons.

The President (Mr. Terence Millin), in summing up, said that Mr. Hanley had emphasized one point, perhaps but little appreciated, namely the high incidence of malignancy within these vesical pouches. Mr. Millin had personally seen 7 cases of such malignancy within the past two years. For this reason he preferred the extravescical type of operation. He endorsed most whole-heartedly the operation described by Mr. Pyrah and, in fact, used it almost exclusively. Where the bladder-neck obstruction was of the median bar type he employed a transurethral resection; where an adenomatous prostate was associated, he carried out a retropubic enucleation, usually at the same time as the diverticulectomy. In certain cases where an adenomatous prostate required intervention and where a relatively small diverticulum was present, he carried out a retropubic enucleation, leaving the diverticulum. If later increase in the size of the pouch or persistent infection seemed to demand a diverticulectomy this could be readily carried out without the well-known disadvantage of such an operation following a transvesical prostatectomy.

[April 28, 1949]

The following cases and specimens were shown:

(1) Bilateral Testicular New Growths. Implantation of Artificial Testes. (2) Innocent Papilloma of the Ureter.—Mr. J. H. CARVER.

Monorchism.—Mr. J. D. FERGUSON.

(1) Total Prostatovesiculectomy. (2) Vesical Papillomatosis with Spread up the Ureter.—

Mr. TERENCE MILLIN.

Megalo-ureter.—Mr. G. J. GRIFFITHS (introduced by Mr. TERENCE MILLIN).

Pedunculated Vascular Tumour of the Ureter.—Mr. WALTER GALBRAITH.

Carcinoma of Ureter.—Mr. STEPHEN POWER.

Bilateral Renal Calculi. Problem for Treatment.—Mr. H. J. MCCURRICH (introduced by Mr. TERENCE MILLIN).

(1) Glands in Nephro-ureterectomy for Tubercle (Child). (2) Inclusion of Intravenous Extension in Removal of Hypernephroma.—Mr. WILFRID ADAMS.

Anaplastic Carcinoma in Calculous Hydronephrosis.—Mr. J. GABE.

[January 28, 1949]

**Nephrocalcinosis in Infancy.**—B. W. POWELL, M.R.C.P. (for P. R. EVANS, M.D., F.R.C.P.)

J. L., male, aged 15 months.

First child of healthy parents. Birth-weight 7 lb. 13 oz. Breast-fed for six months. Soon after weaning was started he began to vomit.

On 13.11.48 (aged 1 year) he was admitted to hospital. Weight 14 lb. 10 oz. (less than at 6 months). Wasted and miserable, with mild dehydration and marked hypotonia. Afebrile. Pulse and respiration rates normal. Feeding was difficult but he appeared to be thirsty. Very constipated.

**Investigations.**—Blood: Serum chlorides 752 mg.%, plasma bicarbonate 34 vol.  $\text{CO}_2$ %. Blood urea 78 mg.%. Serum calcium 10.1 mg.%. Protein 6.8%. Serum sodium 360 mg.%. Serum potassium 25 mg.%. Inorganic phosphorus 3.9 mg.%. Urine: Alkaline. Centrifuged deposit contained 10–20 W.B.C. per microscopic field. Culture: *Proteus vulgaris*. Ammonia coefficient 5%.

Mantoux 1/10,000 negative.

Radiographs: Chest and long bones normal. Abdomen: Calcification in both kidneys (fig. 1). Intravenous pyelogram: Both kidneys excreted the dye.

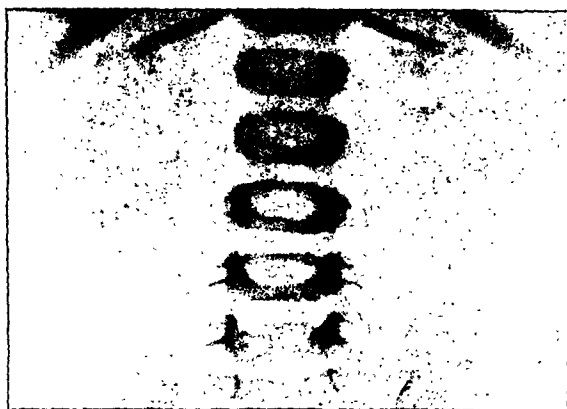


FIG. 1.—Nephrocalcinosis in infancy: calcification in both kidneys.

**Treatment:** A mixture of citric acid 60 grammes, sodium citrate 100 grammes in water to 1 litre; started on 30.11.48 at 60 c.c. *per diem* and increased gradually to 120 c.c. *per diem*.

**Progress:** Marked improvement. On 8.12.48 the serum chlorides were 650 mg.%, plasma bicarbonate 34 vol.  $\text{CO}_2$ % and blood urea 41 mg.%. On 28.1.49 he was continuing to do well and was gaining weight. Blood chemistry: Serum chlorides 609 mg.%, plasma bicarbonate 50.2 vol.  $\text{CO}_2$ %, blood urea 30 mg.%.

**Ollier's Disease (Dyschondroplasia).**—ALEX RUSSELL, O.B.E., M.R.C.P. (for C. T. POTTER, M.D., F.R.C.P.).

Severe case demonstrating

- (a) Extensive bilateral defects with predominant basic unilateral pattern.
- (b) Radiological evolution of lesions.

R. D., male, aged 12 years.

**History.**—Presented when 6 years old with three weeks' history of a limp. Diagnosis based upon tuber-like phalangeal chondromata of left hand and characteristic radio-translucencies in metaphyses of long bones and in other bones preformed in cartilage as follows:

**Left:** Humerus (proximal end). Metacarpals and phalanges. Femur (both metaphyses). Tibia (proximal). Fibula (proximal). First metatarsal and phalanges of big toe. Scapula. Ilium, pubis and ischium.

**Right:** Femur (proximal). Ilium. Phalanges of little finger.

deposit, sometimes small islands of hyaline cartilage may appear. (10) There is a prominent widening of affected bones with thinning of their cortex, and replacement of the cancellous bone and bone-marrow by a fibrous white, gritty, solid tissue. (11) Differential diagnosis must exclude hyperparathyroidism, Ollier's disease, Hand-Schüller-Christian disease and localized lesions affecting one bone. (12) Some cases have been investigated for a parathyroid defect. Such treatment is not necessary.



FIG. 1.—Note position of left eye.

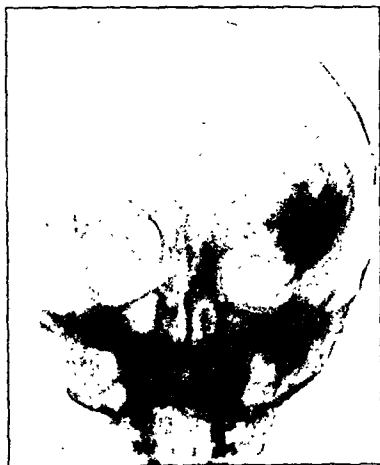


FIG. 2.—Compare appearance with that of fig. 1. Rarefaction of left frontal bone.



FIG. 3.—Trabeculated appearance.

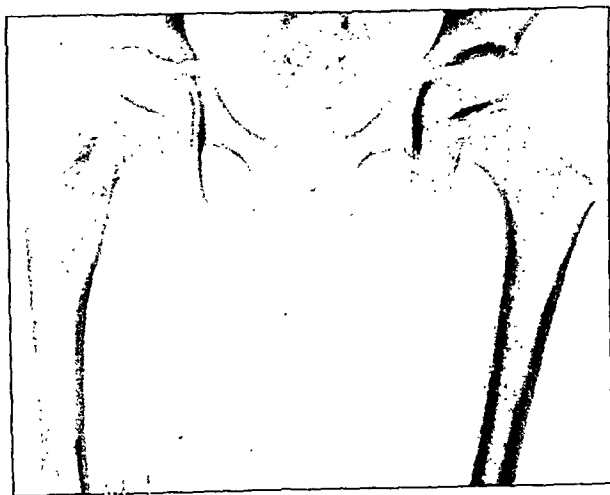


FIG. 4.—Rarefaction upper end of right femur suggestive of cystic disease.

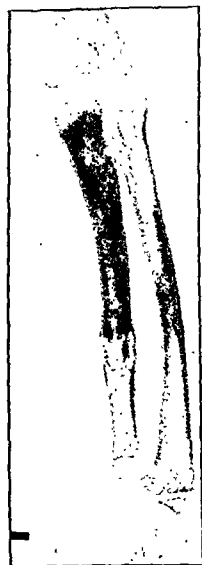


FIG. 5.—Note rarefaction of ulna; absence of lower end.

*Post-mortem* (Dr. W. W. Walther): Liver grossly distorted and covered with a thick layer of perihepatitis; it showed much degeneration and was grossly irregular in outline. The bleeding came from a massive œsophageal varix. Histology (Dr. Doniach): Coarse "Lœnnec" cirrhosis of the liver, and extensive coarse fibrosis of the spleen.



FIG. 1.—Liver: the architecture is disorganized and replaced by "lobules" of liver cells irregular in size and shape, separated and surrounded by thick bundles of fibrous tissue.  $\times 50$ .



FIG. 2.—Spleen: extensive coarse fibrosis, slight lymph-follicle hyperplasia, distended thick walled sinusoids with prominent lining cells.  $\times 50$ .

**Green Teeth Following Icterus Gravis Neonatorum.**—C. W. KESSON, M.D. (for CHARLES PINCKNEY, F.R.C.P.).

C. H., a girl aged 11 months.

*Family history.*—1939: Mother's first pregnancy miscarried at 3 months. No history of preceding blood transfusion. 1945: Second pregnancy normal with spontaneous delivery of live male child at term. This child's progress was uneventful. 1947: Third pregnancy. Hydramnios developed at the 38th week, otherwise uneventful. Maternal Blood-Wassermann and Kahn negative.

12.2.48: Spontaneous delivery at full term of live female child (patient) weighing 7 lb. 10 oz. Jaundice was noticed at birth, the colour rapidly deepened during the first week. On examination two hours after birth there was considerable hepatic and splenic enlargement in association with the jaundice.

Urine contained bile pigment.

Hb 67%, R.B.C. 2,900,000, 18 nucleated red cells per 100 leucocytes. Icterus index 180. Coombs test positive.

Three blood transfusions of Group O Rh-negative blood were required in the first week followed by iron and ammon. cit. gr. iii daily. Breast-feeding was satisfactorily established.

At two weeks the jaundice began to fade and had cleared at 3½ months by which time there was no hepatic or splenic enlargement. The lower central incisors erupted when she was 5 months old and were bluish-green in colour. 8 teeth have now erupted, all of which show a bluish-green pigmentation. There are no abnormal neurological signs, and there has been no delay in her developmental landmarks.

Very rare lesions subsequently becoming evident:

*Left Ribs:* Anterior ends of 6th, 7th, and 8th. Patella (not hitherto recorded).

*Right Ribs:* 2nd and 8th (cystic area).

*First Manifestation:* At 3 years: Swelling of terminal phalanx of left little finger.

*Family history.*—No significant data.

*On examination.*—Mental development normal. Stunting of stature. Conspicuous shortening of left leg (4 in.) and left arm (2 in.). Compensatory lumbar scoliosis. Winging of left scapula mainly due to protrusion of lesions on its inner surface; a feature also occasionally associated with diaphyseal aclasis. No element of hemiatrophy. *Teeth:* Absence of permanent upper lateral incisors—as recorded in several cases. Persistence of deciduous left upper lateral incisors and canines.

*Investigations.*—Urine and blood-count normal. Blood-pressure 105/75. Mantoux 1/1,000 negative.

|                         |            |            |                             |
|-------------------------|------------|------------|-----------------------------|
| <i>Blood chemistry:</i> | 3.642      | 16.642     | 17.149                      |
| Serum phosphorus        | 2.0 mg. %  | 2.2 mg. %  | 4.5 mg. %                   |
| Serum calcium           | 16.7 mg. % | 14.6 mg. % | 9.5 mg. %                   |
| Alk. phosphatase        | 7.7 units  | 7.0 units  | 4.5 (King-Armstrong units). |
| Serum cholesterol       |            |            | 240.00 mg. %                |
| Serum proteins: Total   |            |            | 6.77 %                      |
| Albumin                 |            |            | 4.75 %                      |
| Globulin                |            |            | 2.02 %                      |
| N.P.N.                  |            |            | 33.00 mg./100 ml.           |

*Serological:* W.R. and Kahn negative. Blood grouping: Incompatibility is revealed but no evidence of iso-immunization.

*Patient:* (first child) Group O Rh positive.

*Mother:* Group A Rh negative, no antibodies.

*Father:* Group O Rh positive.

Genotype probably R<sub>1</sub>R<sub>1</sub>

2 Siblings

*Brother:* (10) Group O Rh positive.

*Sister:* (5) Group A Rh positive.

*X-ray studies:* Demonstrate progressive regression of all lesions except chondromata in ribs and phalanges of fingers which in contrast show concurrent acceleration of growth.

*Epiphyses:* Gross speckling of epiphyses, especially proximal epiphysis of tibia (left). This involvement is very rarely seen.

*Progress of case:* Degree of growth failure already evident at 6 years when height 41½ in. (average 46.4 in). Weight 36 lb. (average 47 lb.). At 12 years height 50½ in. (approx. 8 in. less than average, and 3½ in. less than brother 2 years younger), weight 54½ lb.

Stunting of stature is mainly attributed to the rare combination of bilateral femoral defects. The coincidental failure of weight gain remains unexplained.

As the lesions tend to heal spontaneously, the rate of bone growth has also increased, each femur having shown an equal spurt of 2½ in. growth in the last eighteen months.

Amputation of left little finger has been necessitated because of the gross S-shaped deformity, and at present a reconstruction of the first phalanx of the left index (involving a small tibial graft) is contemplated to overcome deformity and ensure effective function.

**Hepatic Cirrhosis Following Neonatal Jaundice (Specimen).—E. HINDEN, M.D., M.R.C.P.**

P. C., the sixth child of healthy parents, was born, deeply jaundiced, on 5.4.44. One sibling was mildly jaundiced, but the seventh child was well. Both parents were Rhesus positive, and the mother's Wassermann reaction was negative.

The jaundice persisted for about four months; then it was noticed that her liver was enlarged, but the spleen could not be felt. At 12 months old she started to suffer from liver insufficiency, with failure to thrive, and with marked fat intolerance. Her liver and spleen were enlarged and hard.

On 18.10.48 she was admitted to hospital suffering from a minor respiratory infection. Her liver and spleen were still enlarged and hard. The following day she sustained a severe hæmatemesis from which she did not recover, in spite of prompt transfusion.

# PROCEEDINGS *of the* ROYAL SOCIETY OF MEDICINE

ISSUED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE

HONORARY EDITORS

ERIC A. CROOK      E. R. CULLINAN

EDITOR

J. M. BROWNE KUTSCHBACH

|                                           |                                 |
|-------------------------------------------|---------------------------------|
| G. S. W. ORGANE (Anæsthetics)             | F. T. RIDLEY (Ophthalmology)    |
| J. S. RICHARDSON (Clinical)               | H. L.-C. WOOD (Orthopædics)     |
| J. B. BROOKSBY (Comparative Medicine)     | C. S. HALLPIKE (Otology)        |
| E. W. PROSSER THOMAS (Dermatology)        | A. G. SIGNY (Pædiatrics)        |
| E. F. SCOWEN (Endocrinology)              | F. R. SELBIE (Pathology)        |
| ALLAN McFARLAN (Epidem. & State Med.)     | M. B. RAY (Physical Medicine)   |
| A. C. WHITE (Exper. Med. & Therap.)       | O. V. LLOYD-DAVIES (Proctology) |
| I. E. McCracken (History of Medicine)     | DENIS HILL (Psychiatry)         |
| W. A. MILL (Laryngology)                  | F. CAMPBELL GOLDING (Radiology) |
| MAURICE DAVIDSON (Medicine)               | CHARLES DONALD (Surgery)        |
| J. St. C. ELKINGTON (Neurology)           | G. M. FINDLAY (United Services) |
| LESLIE WILLIAMS (Obstetrics & Gynæcology) | A. CLIFFORD MORSON (Urology)    |
| B. W. FICKLING (Odontology)               |                                 |

SECRETARY OF THE ROYAL SOCIETY OF MEDICINE

G. R. EDWARDS

25.1.49: Hb 86%, R.B.C. 4,840,000.

Father.—Group O Rhesus positive: genotype CDe/cde

Mother.—Group A Rhesus negative: genotype cde/cde

Baby.—Group A Rhesus positive: genotype CDe/cde

**Spasmus Nutans.**—JOHN BURKINSHAW, M.B., M.R.C.P. (for C. W. KESSON, M.D.).

P. G., boy, aged 9 months. Complaint: Shaking head.

*History.*—Full term; normal labour. Birth-weight 7½ lb. Breast-fed for six months. No vitamin D supplements since age 1/12. At 6 months: Gastro-enteritis followed by "pneumonia". Nursed at home at back of room in basement for two months. Before and after this illness he had been taken out of doors regularly.

Ten days before admission: Noticed to shake his head, especially when not looking at anything in particular. Nystagmus noted in left eye when looking at near objects.

Milestones: Sat up at 6 months. Now standing and crawling. First tooth 8/12.

*Family history.*—Father, mother and three siblings alive and well. No albinos in family. No family history of nystagmus. All siblings have fairer hair than patient.

*On examination.*—Healthy child. Fontanelle widely patent. Four teeth. Weight 20 lb. 6 oz. Heart, lungs, abdomen, normal. C.N.S.: No abnormality except: Nodding of head, most marked when gazing into distance. Tends to glance sideways "out of corner of eyes". Nystagmus of eyes, left much more than right. Movements about 120 to minute. Fine and tending to be rotary. Most marked on looking at a near object.

Fundi (under anæsthetic): Choroidal vessels fairly well seen in both eyes: otherwise normal.

X-ray wrist: No evidence of rickets.

Serum Calcium = 10 mg. per 100 c.c. Phosphorus = 2.9 mg. per 100 c.c. Alkaline Phosphatase = 12.6 units.

**Hemihypertrophy. ? Hæmangioma.**—M. W. ARTHURTON, M.R.C.P. (for DAVID LEVI, M.S.).

J. M., male, aged 4 years.

*History.*—First seen on 16.10.45. Only child of healthy parents. No relevant family history. Milestones normal. Teeth of left upper jaw erupted later than the remainder. Prominence of left eye and asymmetry of face noted at birth, since when no definite change has been observed. Port-wine stains on trunk seen in early life. Injuries sustained to right leg have resulted in ½ in. shortening of right tibia and ununited fracture of right fibula.

*On examination.*—Marked left-sided proptosis with œdema of lids. Enlargement of left ear, eye, cornea and pupil. No bruit heard over left upper lid. Left pupil irregular and reacts sluggishly to light. Both fundi normal. Appears to see with left eye. Acuity not measured. Left side of nose longer than right. Teeth of left upper jaw widely spaced and partly hidden by enlargement of left hard palate. No protrusion of upper incisors. Arms equal in length. Valgus deformity of left ankle. Chest and trunk symmetrical. Systolic murmur without thrill maximal in fourth left intercostal space ½ in. lateral to left side of sternum.

*Investigations.*—W.R. negative. Biopsy of suboccipital gland histologically normal. X-rays of skull show enlargement of left orbit and pituitary fossa, and dilatation of foramina of middle cranial fossa. No bony erosion seen.

POSTSCRIPT.—Mr. David Levi has since carried out a biopsy of the left cheek which histologically showed a plexiform neurofibroma.



# PROCEEDINGS *of the* ROYAL SOCIETY OF MEDICINE

ISSUED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE

HONORARY EDITORS

ERIC A. CROOK      E. R. CULLINAN

EDITOR

J. M. BROWNE KUTSCHBACH

|                                           |                                 |
|-------------------------------------------|---------------------------------|
| G. S. W. ORGANE (Anæsthetics)             | F. T. RIDLEY (Ophthalmology)    |
| J. S. RICHARDSON (Clinical)               | H. L.-C. WOOD (Orthopædics)     |
| J. B. BROOKSBY (Comparative Medicine)     | C. S. HALLPIKE (Otology)        |
| E. W. PROSSER THOMAS (Dermatology)        | A. G. SIGNY (Pædiatrics)        |
| E. F. SCOWEN (Endocrinology)              | F. R. SELBIE (Pathology)        |
| ALLAN McFARLAN (Epidem. & State Med.)     | M. B. RAY (Physical Medicine)   |
| A. C. WHITE (Exper. Med. & Therap.)       | O. V. LLOYD-DAVIES (Proctology) |
| I. E. McCracken (History of Medicine)     | DENIS HILL (Psychiatry)         |
| W. A. MILL (Laryngology)                  | F. CAMPBELL GOLDING (Radiology) |
| MAURICE DAVIDSON (Medicine)               | CHARLES DONALD (Surgery)        |
| J. St. C. ELKINGTON (Neurology)           | G. M. FINDLAY (United Services) |
| LESLIE WILLIAMS (Obstetrics & Gynecology) | A. CLIFFORD MORSON (Urology)    |
| B. W. FICKLING (Odontology)               |                                 |

SECRETARY OF THE ROYAL SOCIETY OF MEDICINE

G. R. EDWARDS



NEW PRESENTATION  
25 mg. Glossettes.

REDUCTION IN PRICE  
of 5 mg. Glossettes.

# METHYLTESTOSTERONE

GLOSSO-STERANDRYL 25 mg. (ROUSSEL)

SUBLINGUAL ADMINISTRATION

NOW IN TWO STRENGTHS

5 mg. and 25 mg.

## ADVANTAGES OF THE 25 mg. GLOSSETTES

**Small Doses:** One 25 mg. Glossette per day, instead of five 5 mg. obviates the inconvenience of having to retain them in the mouth for a period five times as long.

**High Doses:** Until now, there has been no convenient method for the sublingual administration of high doses of male hormone. This is now possible using repeated daily administration of the 25 mg. Glossettes.

*IN THE MALE: Hypogonitalism, Male climacteric, Senility.*

*IN THE FEMALE: Metrorrhagia, Premenopausal disorders.*

5 mg. Glossettes: 20...12/9, 100...57/6, 500...266/-  
25 mg. Glossettes: 10...28/-, 20...56/-, 100...252/- 250...610/-



ROUSSEL LABORATORIES LIMITED  
4 Golden Square, London, W.1 GERard 3111/2

# PROCEEDINGS

## OF THE

# ROYAL SOCIETY OF MEDICINE

Vol. XLII    No. 8    August 1949

## CONTENTS

Whole  
Proceedings  
Page

### Section of the History of Medicine

- Galen as a Modern.—CHARLES SINGER, M.D. . . . . 563

### Section of Dermatology

*February 17, 1949*

- Lupus Vulgaris, Resistant to Calciferol. Treated with Streptomycin and Calciferol.—  
R. M. B. MACKENNA, M.D., and BRIAN RUSSELL, M.D. . . . . 571

*March 17, 1949*

- Werner's Syndrome.—DAVID I. WILLIAMS, M.R.C.P. . . . . 572  
Dermatitis Herpetiformis with Ocular Manifestations.—P. J. HARE, M.B., for  
W. N. GOLDSMITH, M.D. . . . . 573

### Section of Physical Medicine

*February 9, 1949*

- DISCUSSION ON NEUROLOGICAL ASPECTS OF RHEUMATIC DISEASES . . . . . 575

*May 11, 1949*

- Electrodiagnosis and Electrotherapy in the Royal Air Force . . . . . 582  
Some Aspects of Electrodiagnosis and Electrotherapy in the Royal Air Force.—  
Squadron-Leader E. F. MASON, M.B.E., M.B., Ch.B., D.Phys.Med. . . . . 582  
Clinical Electromyography in the Royal Air Force.—Flight Lieutenant A. T.  
RICHARDSON, M.B., B.S. . . . . 587

### Section of Orthopaedics

- Arthritis of Wrist Relieved by Synovectomy.—M. C. WILKINSON, M.B. . . . . 593  
Osteotomy of the Spine in the Treatment of Severe Dorsal Kyphosis: Four Cases.—  
W. ALEXANDER LAW, O.B.E., M.D., F.R.C.S. . . . . 594  
Comminuted Fracture-Dislocation of the Shoulder: Result Seven Years After Excision  
of Fragments and Treatment on Abduction Splint.—L. S. MICHAELIS, M.D. . . . . 597  
Traumatic Genu Recurvatum.—DAVID TREVOR, M.S. . . . . 599  
Congenital Deformity of Wrists.—R. C. F. CATTERALL, F.R.C.S. . . . . 600  
Neuropathic Joint Showing a Fracture of the Lower End of the Right Femur and Internal  
Condyle of the Right Tibia Both Involving the Knee-joint.—W. E. TUCKER,  
M.B.E., F.R.C.S. . . . . 600  
Spondylolisthesis with Bilateral Drop Foot.—G. P. ARDEN, F.R.C.S. . . . . 601

### Section of Neurology

- Traumatic Changes in the Brain after Spontaneous Delivery at Full Term.—  
Professor B. BROUWER . . . . . 603

### Section of Ophthalmology

- Anterior Retinal Dialysis.—C. DEE SHAPLAND, F.R.C.S. . . . . 609

### Section of Experimental Medicine and Therapeutics

*March 8, 1949*

- DISCUSSION ON ANTIHISTAMINE DRUGS. . . . . 615

*May 31, 1949*

JOINT MEETING WITH THE MEDICAL SOCIETY FOR THE  
STUDY OF VENEREAL DISEASES

- Recent Advances in the Study of Venereal Disease. [*Abstracts*].—JOSEPH EARLE  
MOORE, M.D. . . . . 629

(Continued on next page)

## Section of Paediatrics

February 25, 1949

DISCUSSION ON PLANNING A PEDIATRIC UNIT IN AN UNDERGRADUATE TEACHING HOSPITAL  
(WITH A TRAINING SCHOOL FOR NURSES). [*Abridged*] .. .. . 631

March 25, 1949

A Pattern of Disease in Infancy. Based on 2,306 Hospital Admissions in the Years  
1946-48 Inclusive.—President's Address by Professor J. M. SMELLIE, O.B.E., M.D.,  
F.R.C.P. .. .. . 636

(N.B.—The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.)

**Copyright:** The Society holds the copyright of all matter accepted for publication in the *Proceedings*. Requests for subsequent publication elsewhere should be made to the Honorary Editors. All papers, &c., presented at meetings (other than those which have been previously published) are held to be subject to the Society's copyright until a decision in regard to their publication has been made.

**Digests:** Requests for permission to make Digests from the *Proceedings* should be addressed to the Honorary Editors.

All communications concerning Editorial Business should be addressed to  
THE HONORARY EDITORS, 1, WIMPOLE STREET, LONDON, W.1

Applications for advertisement space in the "*Proceedings*" should be made to the Society's official advertising agents,  
Messrs. C. Mitchell & Co. Ltd., Mitchell House, 1 and 2, Snow Hill, London, E.C.1.

Copies of the whole *Proceedings* may be purchased through any bookseller. Prices are as follows:—

|                                                                  |                           |
|------------------------------------------------------------------|---------------------------|
| Single copies                                                    | 10s. 6d. each, post free. |
| Annual subscription, covering 12 monthly issues and annual index | £6 6s. 0d.                |

Reprints of Sectional parts may be obtained direct from the Society. Prices are as follows:—

|                     |                          |
|---------------------|--------------------------|
| Single copies       | 3s. 6d. each, post free. |
| Annual subscription | 15s. 0d.                 |

Fellows and Members of the Royal Society of Medicine are asked to apply direct to the Society for any copies of the *Proceedings* they may require, whether whole or Sectional, in addition to those they receive *gratis*. Prices are as follows:—

**Whole *Proceedings*:**

|                                                      |                          |
|------------------------------------------------------|--------------------------|
| Single copies                                        | 7s. 6d. each, post free. |
| Complete volume (12 monthly issues and annual index) | £5 0s. 0d.               |

**Sectional *Proceedings*:**

|                     |                          |
|---------------------|--------------------------|
| Single copies       | 3s. 0d. each, post free. |
| Annual subscription | 10s. 0d.                 |

## Publication Rules.

**Copyright:** The Society holds the copyright of all matter accepted for publication in the *Proceedings*. Requests for subsequent publication elsewhere should be made to the Honorary Editors. All papers, &c., presented at meetings (other than those which have been previously published) are held to be subject to the Society's copyright until a decision in regard to their publication has been made.

**Digests:** Requests for permission to make Digests from the *Proceedings* should be addressed to the Honorary Editors.

**Manuscripts** should be concise and *carefully revised for press*. They must be top copies, typewritten in double spacing, with the author's name, degrees and address on the first page. A carbon copy should be retained by the author.

The text must contain references to all tables and illustrations; these should be numbered and packed separately.

Dosages and other measurements should be given in metric units.

**References:** The Harvard system should be followed, i.e. each work should be cited in the text by the author's name and date of publication, and at the end of the paper a list should be given in alphabetical order according to the authors' names. Names of journals should be abbreviated in accordance with the "World List of Scientific Periodicals", e.g.

ATKINSON, J. (1921) *J. biol. Chem.*, 47, 134.

With the title of a book the name of the publisher and the place of publication should be given.

**Illustrations** should be numbered consecutively and the top clearly marked. They must be suitable for direct photographic reproduction.

Photographs should be glossy prints. *No negatives or slides will be accepted*. The important feature of each photograph should be indicated, preferably by pencil lines on the back.

All numerals, &c., appearing on diagrams should be large and bold to allow of reduction in size.

**Blocks** used for the illustration of articles in the *Proceedings* will be presented to authors shortly after each volume is concluded.

**Reprints** may be obtained from the Society's printers, Messrs. Staples Press Limited, 83-91, Great Titchfield Street, London, W.1.

## Section of the History of Medicine

President—E. ASHWORTH UNDERWOOD, M.A., M.D., D.P.H.

[June 1, 1949]

### Galen as a Modern

By CHARLES SINGER, M.D.

A FEW preliminary words on certain obvious debts of modern medicine to Galen.

Firstly, the earliest modern anatomies were based on his work. Our anatomical nomenclature is essentially his. Many of our commonest anatomical terms were taken direct from him. Some of his terms came into our anatomical vocabulary in the thirteenth/fourteenth century, most in the sixteenth century, a few since.

Secondly, he is the undisputed ancestor of experimental physiology. The very basis of modern medicine, the conception that rational treatment can be determined only by our view as to the actual workings of the body, comes to us from him. Could any higher claim be made for him as one of the moderns?

Thirdly many vegetable drugs still in use were recommended by him. Pharmacists, when they make up prescriptions, still refer to their vegetable ingredients as *galenicals*. The origin of this term is not far to seek, for the stock therapeutic textbook that was in use for many centuries was a Latin translation of one of his works. All modern pharmacopœias have been influenced by it.

But if Galen is so far a Modern, it is also true that we are separated from him by a whole universe of discourse. That which especially cuts us off from him is not in the practical region of rational medicine; it belongs rather to the field of ultimate belief, of religion if you will. Whatever we think of the nature of life, we can hardly begin to understand Galen's conception of it without some philosophical discussion. His view is obscure to us because our fundamental attitude to the physical world is incompatible with his. For Galen adhered—somewhat loosely, it is true—to the Stoic creed of his master and friend, the philosopher-emperor Marcus Aurelius. The essential feature of their faith was belief in the existence of a world-spirit or *world-pneuma*. This must not be confused either with the Christian conception of *spirit* or with the chemical conception of vapour or gas. Yet Christians and chemists and Christian chemists have all made this confusion, times out of number.

The idea of *pneuma* carries with it the thought, sound, and meaning of the act of breathing. It involves, too, the idea that there is something drawn in with every breath. But what is that something, and in what sense is it "material", and what do we mean by "material"? How can these things be answered here? How many generations of philosophers and theologians have dreamed of the nature of that which God breathed into the nostrils of the first man? How many have failed to make their dreams intelligible? I will not enter the discussion of the meaning of *spirit* in Holy Writ, but the *pneuma* of classical antiquity involved a conception of the nature and meaning of breathing utterly different from our view that treats breathing as subserving the oxygen-carrying functions of hæmoglobin.

The Ancients in general and the Stoics in particular did not regard air as having weight. They knew nothing of the nature and variety of gases. Those ideas (like the word "gas" itself) date from the seventeenth century (with perhaps certain earlier adumbrations). The Stoics of old believed in a general *world-pneuma* or *world-spirit* which we all share during life, manifesting it by our breathing. At our death, when we cease to breathe, our share passes to join again the general world-spirit from whence it was first drawn. So much can be learned from the sweetly-sad *Meditations of Marcus Aurelius*, truly and literally an *inspiring* work. There are passages in its lovely pages which make the reader draw his breath deeper.

The physiologists of antiquity, personified by Galen, had their own ways of explaining the incarnation of this spirit in the body of man. Galen would trace its transformation into the *natural spirit* which was made in the liver and was distributed by its branches, the veins; this in turn was transformed into *vital spirit* which was elaborated in the (left) heart and was distributed thence by its branches, the arteries; and this finally was transformed into *animal spirit* by the action of (the *rete mirabile* of) the brain, whence it was distributed by the nerves. We have no need to follow further the Pneumatics of Galen. It is enough for the present to remember that Galen ascribed all activities of living things to such manifestations of the world-spirit. That was essential to his outlook on the organism. From that outlook he could as little rid himself as we can of our conception of the chemical action of digestive processes or the mathematical relationships of mechanical devices. In his physiological work, Galen was always dealing with some incarnation of this world-spirit. But while doing so he strove, as earnestly as any modern physiologist, to explain the actual workings, the mechanical apparatus, of the body. It is this effort that brings him among the moderns. Once we have realized this, we are no more concerned with his philosophy than we need be with the religion of a modern physiologist. Philosophy and science are on different levels of thought. Unless we can separate them we can have no science. Among the intellectual results of failure to separate them was the collapse of science after Galen and the mental confusion of the centuries that follow. Of course I do not suggest that this was the only cause of the darkness of the Dark Ages.

Galen began writing when he was 13. He wrote rapidly, easily, and constantly till he died at 70. The bulk of his works is truly portentous. It covers, indeed it smothers, the medicine of antiquity. If we omit the *Corpus Hippocraticum*, Galen represents at least five-sixths of all the medical writings surviving from antiquity. Most of the ancient medical writers after Galen do little but repeat him. His works occupy twenty-two thick octavo volumes in the standard modern edition. In actual words Galen probably exceeds Aristotle or Plato.

It is unlikely that anyone now living has read all Galen, either in the original or in translation, nor is there any very obvious reason why anyone should. Our debt to him is great, but he was always intolerably verbose, often unbelievably credulous, and usually maddeningly repetitious. He has no literary charm. Some of what he wrote is little better than nonsense. It is hard to believe that his philosophical writings have value in themselves, but they do reflect a way of thinking that was historically significant and they are also interesting as containing certain references to the Christian and Jewish scriptures, for he is the first pagan to mention them with any knowledge or respect. Of his works as a whole it may fairly be said that had he condensed them into one-twentieth of their space, he would now be studied twenty times more frequently. But he was no condenser.

I have called Galen a *Modern*. Why modern? Because his conception of disease is anatomic. All progress in medicine is ultimately reducible to anatomic terms. As men learn more of the organism, of its workings as a mechanism or as a laboratory, of the nature of its defects, diseases, and infections, their views become ever more

minutely and exactly expressed in anatomic terms. That is the way of modern medicine; but it is not the way of medicine that is really ancient. In this respect consider the "Hippocratic" writings. Their authors treat the body as a mingling of the four elements, earth, air, fire and water, or rather of their surrogates, the four humours, blood, phlegm, black bile and yellow bile. The idea is traceable back to Empedocles (c. 500 B.C.—c. 430) but is doubtless much older than he. Humoral medicine is really ancient medicine. The anatomic view is relatively modern and persistent adhesion to it places Galen among the moderns. When the anatomic view first became possible, we shall presently discuss.

Soon after Galen's death his anatomical and physiological works were lost to the Latin West. They remained unknown till the thirteenth century when they began to be translated into Latin. They were, however, grossly misunderstood till the sixteenth. Greek or Arabic MSS of (almost) all of them had been recovered by the Latins by the end of the fifteenth century and by about 1550 they had all become fully available in printed Latin translations. It would be easy to present the progress of medicine from then till now as an extension of Galen's line of anatomical thought as revealed in the Latin versions. For him disease was located in a particular spot or spots of the body, that is to say it must be anatomic. But to this day there linger some traces of the pre-Galenic humoral pathology. We still speak of men as "sanguine", "choleric", "melancholy" or "phlegmatic" and often find our patients "temperamental"—all merely old names for the humours and their mixture. Not long since physicians commonly spoke of the "constitutions" of their patients, that is of their humoral make-up. *Every Man in his Humour* is a title chosen by a not unknown dramatist (Ben Jonson, 1598) and we still suffer from the too *humorous* fellow. These are survivals of pre-Galenic ideas. Indeed Galen himself was far from freeing himself from these ideas, but our claim for him is that he, like us moderns, was moving away from them.

It is about as sure as anything of the sort can be that the earlier Greek writers, and notably those of the Hippocratic Corpus, had learned nothing of the anatomy of the human body by dissection. Even Aristotle (died 322 B.C.), despite his biological preoccupations, was as ignorant of human anatomy as his Hippocratic forebears. When then did Medicine begin to become modern? The answer is in Alexandria about 300 B.C. There and then Medicine took a step more revolutionary than any that it has taken since. It was there and it was then that human anatomy began to be studied.

For how long and where was human dissection practised in antiquity? This question is less easy to answer exactly because Alexandrian scientific literature has been lost. Galen's medical education began in A.D. 146. He never saw a human dissection. I know no evidence that any of his teachers had done so. In Galen's study years there did, however, linger a tradition of practical anatomy. Galen knew of it at Corinth, at Smyrna and at several other East Mediterranean centres, but especially at Alexandria. The practice of human dissection had, however, ceased even there by about A.D. 100. The ecclesiastical writer Tertullian, who was about contemporary with Galen, expresses horror at human dissection but in such a way as to suggest that it was a distant memory in his day.

The word *galenos* means "calm", "peaceful" and it was his given name. It was peculiarly inappropriate to him, for he was a most contentious and bitter controversialist. We have no authority for his other name or names. *Claudius*, often attached to Galen, has arisen from a misunderstanding. Some Renaissance scholar seems to have thus misread an abbreviated epithet such as *cl.* for *clarissimus*. Claudius Galen should disappear from literature.

Galen's father Nikon was an architect, a philosopher, and man of ample means which he transmitted to his son. Galen apparently was always independent of his

profession for his livelihood and he could always afford ample material for his experiments. He was born at Pergamum, one of the most beautiful Hellenistic cities, an important cultural centre with a library second only to that of Alexandria. It is referred to in the Apocalypse of John the Divine as *Satan's Throne* (Ch. II, 12-17). This, it seems to me, may be a natural metaphor for the great amphitheatre attached to the shrine of Æsculapius or for the magnificent terracing of the public buildings leading up to the Acropolis—compare “King Arthur's Seat” or “The Devil's Punchbowl”. In any event Pergamum was both the seat of the greatest cult of Æsculapius in Asia Minor and also of one of the Seven Churches to which John was bidden to write. Galen must have known of the Christian and perhaps of the Jewish community there from his earliest years. Hence perhaps his knowledge of their scriptures.

Galen attended the medical school of his native town from his sixteenth to his nineteenth year and he lived three years longer at Smyrna where there was a teacher of anatomy. He then visited Corinth where he found that anatomical knowledge was fading and he completed his medical education by five years of study at Alexandria. He saw no human dissection there but he obtained a good practical knowledge of the human skeleton and in later years he recommended students to go there to study human bones. From Alexandria he returned to Pergamum where he remained for four years as surgeon to the stadium, attending the gladiators and athletes. He thus became expert in treating sprains, fractures, dislocations and wounds.

At 33 he went to Rome and settled there in practice for three years. Despite, or perhaps because of, his sound training and surgical experience he had difficulty with his professional colleagues and he came to practise rather as physician than surgeon. In A.D. 166 he left Rome for a prolonged journey in the Near East, visiting Cyprus, Syria and Palestine and his native Pergamum. He tells nothing of calling at Athens. This is a strange omission for Marcus Aurelius had endowed the school of philosophy there. His record of his journey to Palestine is rather disappointing. He returned to Rome in 169 and remained there until his death, serving under four Emperors: Marcus Aurelius (161-180), Commodus (180-192), Pertinax (193) and Septimus Severus (193-211). He was the friend of the first and the constant personal attendant of the second.

As to his works: They may be crudely divided into (a) general, personal and philosophical, (b) therapeutic and clinical and (c) anatomico-physiological and pathological. We are concerned here only with the third class. For historical purposes the Latin translations of these are more directly significant than the Greek originals. Very few—perhaps none—of the effective anatomists of the sixteenth century had any real facility in Greek, though there was a general pretence to Greek learning among them. The most important of Galen's works for the influence that they ultimately exerted are the following, of which we give the conventional titles in their Latin forms:

(1) *De iuvamentis membrorum* (“On the functions of the members”). It is the real foundation of modern anatomy since it was used by Mundinus (died 1318), the first modern who wrote on human anatomy. The *De iuvamentis* is not a translation of any text of Galen but a Latin abstract of (2). It was made by some unknown writer in the thirteenth century probably from an Arabic version. First edition, Pavia 1516.

(2) *De usu partium corporis humani*. (“On the actions of the parts of the human body”). Latin translation by Nicolas of Reggio c. 1310. A fairly well-arranged complete textbook of anatomy and physiology containing numerous and remarkable observations and experiments. It was written before (3). It provided the basis of anatomical reading in the universities until Vesalius in the sixteenth century. First edition, Pavia 1516.



(3) *De anatomicis administrationibus*. ("On anatomical procedures".) Originally in sixteen books of which the last seven were early lost (in the original Greek) and therefore failed to influence anatomy. The first nine were printed in Greek at Paris in 1531, and translated into Latin by Guenther of Andernach and printed at Paris in the same year. It made a deep impression on his pupil Vesalius and formed, with (2), the foundation of his work and, through him, of modern anatomy. The *De anatomicis administrationibus* is really a laboratory handbook of actual anatomic findings.

(4) and (5) *De venarum arteriarumque dissectione; De nervorum dissectione*. ("On the dissection of the veins and arteries . . . and nerves".) These small books are little but extensions of (3). Both were first translated and printed at Paris in 1526 and both were used by Vesalius.

(6) *De ossibus ad tirones*. ("On bones for students".) Important because it is the only work of Galen, and indeed the only anatomical work of antiquity, based on human material. It was first translated and printed at Paris in 1535.

(7) *De musculorum motu*. ("On the movements of the muscles".) First translated by Nicolo Leonicensio and printed in London in 1522. It forms the basis of the muscular physiology of Vesalius and with it of the whole modern science of orthopaedics.

(8) *De musculorum dissectione ad tirones*. ("On dissection of muscles for students".) An excellent work in a positive modern spirit, less verbose than most of Galen's. It makes a good companion to (7) but it was not accessible until edited by Agostino Gadaldino, Venice 1550, and was therefore too late to be used by Vesalius. It thus had relatively little effect on modern anatomy.

(9) *An secundum naturam in arteriis sanguis continetur*. ("Whether there is blood in the arteries in their natural state".) Perhaps the earliest of Galen's works on experimental physiology. It was edited in Latin by Guenther of Andernach, Paris 1536.

(10) *De utilitate respirationis*. ("On the use of respiration".) Contains experiments on penetration of the pleura and artificial respiration with bellows. It became available in the Latin version of Janus Cornarius, Basel 1536.

(11) *De facultatibus naturalibus*. ("On the natural faculties".) Contains some account of Galen's physiology. Unfortunately it is exceptionally argumentative and flatulent. It first became available in the Latin translation of Thomas Linacre, London 1523. It is the only work of Galen adequately rendered into English. (See the edition of A. J. Brock in the Loeb Library, London 1916.)

(12) *De locis affectis*. ("On disordered parts", "On the sites of diseases" as we might say.) An important work which deeply affected medical ideas of the sixteenth and following centuries. A Latin translation by Guglielmo Copo appeared at Venice in 1500. (The Greek text was not printed until 1554.) It merits respect as the first attempt at an anatomical pathology.

Galen's anatomical knowledge was based on the dissection of a very large number and variety of creatures, both living and dead, apes of several species, pigs, sheep, oxen, cats, dogs, weasels, bears, mice and at least one elephant. Invertebrates were beyond him for he had no magnifying glass. Roughly speaking, we may say his anatomy is that of the soft parts of the Barbary ape, *Macaca Inuus*, imposed on the human skeleton. His physiological experiments were made on ungulates and apes. For anatomy the ape was a good choice for the surgery of his time, which was hardly concerned with the inner organs. For ordinary surgical instruction it was better for students to have plenty of freshly killed apes than a few unpreserved human bodies. There was no way of making anatomical preparations more permanent and the mere bulk of the human body would have made dissection too slow a process to be effective. Perhaps even in the sixteenth and seventeenth centuries much anatomy would have been better taught on apes.

profession for his livelihood and he could always afford ample material for his experiments. He was born at Pergamum, one of the most beautiful Hellenistic cities, an important cultural centre with a library second only to that of Alexandria. It is referred to in the Apocalypse of John the Divine as *Satan's Throne* (Ch. II, 12-17). This, it seems to me, may be a natural metaphor for the great amphitheatre attached to the shrine of Æsculapius or for the magnificent terracing of the public buildings leading up to the Acropolis—compare “King Arthur's Seat” or “The Devil's Punchbowl”. In any event Pergamum was both the seat of the greatest cult of Æsculapius in Asia Minor and also of one of the Seven Churches to which John was bidden to write. Galen must have known of the Christian and perhaps of the Jewish community there from his earliest years. Hence perhaps his knowledge of their scriptures.

Galen attended the medical school of his native town from his sixteenth to his nineteenth year and he lived three years longer at Smyrna where there was a teacher of anatomy. He then visited Corinth where he found that anatomical knowledge was fading and he completed his medical education by five years of study at Alexandria. He saw no human dissection there but he obtained a good practical knowledge of the human skeleton and in later years he recommended students to go there to study human bones. From Alexandria he returned to Pergamum where he remained for four years as surgeon to the stadium, attending the gladiators and athletes. He thus became expert in treating sprains, fractures, dislocations and wounds.

At 33 he went to Rome and settled there in practice for three years. Despite, or perhaps because of, his sound training and surgical experience he had difficulty with his professional colleagues and he came to practise rather as physician than surgeon. In A.D. 166 he left Rome for a prolonged journey in the Near East, visiting Cyprus, Syria and Palestine and his native Pergamum. He tells nothing of calling at Athens. This is a strange omission for Marcus Aurelius had endowed the school of philosophy there. His record of his journey to Palestine is rather disappointing. He returned to Rome in 169 and remained there until his death, serving under four Emperors: Marcus Aurelius (161-180), Commodus (180-192), Pertinax (193) and Septimus Severus (193-211). He was the friend of the first and the constant personal attendant of the second.

As to his works: They may be crudely divided into (a) general, personal and philosophical, (b) therapeutic and clinical and (c) anatomico-physiological and pathological. We are concerned here only with the third class. For historical purposes the Latin translations of these are more directly significant than the Greek originals. Very few—perhaps none—of the effective anatomists of the sixteenth century had any real facility in Greek, though there was a general pretence to Greek learning among them. The most important of Galen's works for the influence that they ultimately exerted are the following, of which we give the conventional titles in their Latin forms:

(1) *De iuvamentis membrorum* (“On the functions of the members”). It is the real foundation of modern anatomy since it was used by Mundinus (died 1318), the first modern who wrote on human anatomy. The *De iuvamentis* is not a translation of any text of Galen but a Latin abstract of (2). It was made by some unknown writer in the thirteenth century probably from an Arabic version. First edition, Pavia 1516.

(2) *De usu partium corporis humani*. (“On the actions of the parts of the human body”). Latin translation by Nicolas of Reggio c. 1310. A fairly well-arranged complete textbook of anatomy and physiology containing numerous and remarkable observations and experiments. It was written before (3). It provided the basis of anatomical reading in the universities until Vesalius in the sixteenth century. First edition, Pavia 1516.

"Galen here employed monkeys, also young pigs in which he was able to cut through the spines and laminae with a strong knife. In monkeys he passed a fine, flat-bladed knife between the laminae, so as to cut across the cord transversely. To divide the spinal cord longitudinally, after removing spines and laminae, he raised the *dura mater* on a hook so as to incise it without wounding the *pia mater*. He then could cut the cord exactly along the middle line with a fine knife; there was no disturbance of function, neither the intercostal nerves nor the nerves to the hind limbs were paralysed.

"When the cord was divided transversely, the nerves connected with the spinal cord below the division lost the function both of sensation and of motion. If the section was at the level of the sacrum, sensation and motion were lost in the foot, and as the section was made higher up, so there was loss of sensation and of motion in the thigh, the hip and lumbar region. When the section was made at the level of the thoracic vertebrae, the forcible respiratory movements of the animal began to weaken. When the section was just below the middle of the dorsal region, movement continued in the upper intercostals, the upper accessory muscles of respiration and the diaphragm. Galen also noticed that the *Serratus posticus inferior* has a high nerve supply, an observation only confirmed in recent years.

"In monkeys, so long as the section was below the second intercostal space, power in the arms was preserved. A section just above this level caused loss of sensation in the skin of the axilla and inner side of the arms, i.e. in the distribution of the intercosto-humeral nerves. The hands of the monkey were weakened when the section was made at the level of the first rib. When the section was between the seventh and eighth cervical vertebrae, the forearms were weakened but the action of the accessory muscles of respiration continued. By a section at the level of the fifth cervical vertebra the arms were completely paralysed; the diaphragm continued in full movement, also the scaleni, whilst all the intercostal movement was lost."

Galen's career presents a unique phenomenon in the history of science and one perhaps unique in cultural history as a whole. Nearly every exhibition of human activity seems to go through a process of development, flowering, and decline. The Ancients, even the most scientific of them, were not generally great hands at experiment, and Galen represents the climax and flower of the experimental spirit in antiquity, certainly so far as the biological disciplines are concerned. He brought experimental physiology to a very high standard indeed, but he was quite without successors. There is no fading out of physiological activity. It simply disappears. Yet Galen was no solitary worker; he was constantly demonstrating his experiments to large audiences of colleagues and he had many pupils, but he had no followers or imitators. Ancient science fell dead with Galen.

Why was so triumphant a scientific career devoid of successors and even of imitators? This cannot be answered completely, but some inkling of the form that the answer will one day take may perhaps be reached by considering the intellectual associations of his age. The intellectual climate was certainly against experiment. The prevailing philosophy of the educated classes in Italy was Stoicism. This gave no warrant for or encouragement to the investigation of Nature. True, Galen's own thought was based on Stoicism, but he was neither an orthodox Stoic, nor had he the characteristic Stoic temper. The outlook of the Stoic was essentially fatalistic. It had developed a close alliance with the "astrology" of the time. In those days astrology was no idle superstition but a natural development of the ancient cosmology. It had crystallized into a rigid system of beliefs concerning the nature of events on our Globe under the mechanical working of the heavens that surrounded it. Man was enclosed within a spherical machine. Against it he could do nothing and all that he was and did and became was determined by it. There was a Supreme Power, but He was no pitying God nor would He control that pitiless machine. Perhaps God was the Spherical

Galen exhibits a quite surprising knowledge of comparative anatomy. He has a better insight into that subject, on coarse macroscopic lines, than is possessed by most medical men of our own time. He can correlate skull structure with form of foot, teeth with abdominal viscera, and so on. He knows of a considerable variety of apes and distinguishes carefully those which are dog-like—the baboons—from those which have a human form—the macaques. He knows how the differences in the gait of the two types can be expressed as differences in the skeleton and musculature of the lower limb. Among “man-like apes” he distinguishes those with tails and those without. This latter class, which he describes, does not include the “Anthropoids” of modern zoologists but contains only *Macaca Inuus* and a few others. He had never seen an anthropoid ape and statements to the contrary that have been made are due to misunderstanding.

He probably practised mostly on tailed apes, much like the organ-monkeys of our time. These were common in the markets of Rome where his experimental work was done. His favourite form was, however, the tailless Barbary ape, *Macaca Inuus*. A word may be in keeping here as to this scientific term. *Inuus* is a name of the god Pan. By exception to the usual rule of specific names, it is not an adjectival form in agreement with the generic name but a proper name in apposition to it. The accepted designation dates from Lacépède (1799). It corresponds in part to the *Simia sylvanus* of Linnaeus (1758). To me it seems probable that Galen was usually forced to rely on one of the species of Indian macaques which were commoner, even in his time, hardier, more tolerant of captivity and much easier to handle than his favourite Barbary ape.

It is not my purpose to discuss Galen's anatomical terms, but there is one on which perhaps it is well to warn the reader, for it is very misleading. It is sometimes said that Galen failed to distinguish nerves from tendons. This is not the case, but he did hold to a false physiological theory of the nature of tendons which has confused modern readers. In the translations of his texts the Greek word *neuron* (Latin *nervus*) is sometimes translated “tendon” or “sinew” and sometimes “nerve”. Now there is a reason for this. Galen saw that a nerve passes into each muscle and he traced its divisions till they disappeared from sight. He also saw that many muscles terminate in a whitish cord or tendon. He wrongly thought that the branches of the nerves reunite within the muscle to form this structure which he naturally also called *neuron*. His error entails considerable strain on the translator who wishes to be both faithful to his original and intelligible to his reader. Similarly the translator has to contend with the difficult terminology of Galen's pneumatic views.

Of Galen's actual physiological discoveries we have space to refer only to two. Deservedly the most famous is that of the Recurrent Laryngeal Nerves and their action. Indeed his whole section on the voice and its organs in the *De usu partium* (Book VII, Chapters 11 to 18) is among the glories of experimental biology. Incidentally Galen, who seldom fails to praise himself, here exults at immense length over those whom he has there refuted. These held, with the Ancients, that the voice came from the lungs *via* the trachea. The voice of a patient having been injured by an operation (apparently on the thyroid) Galen demonstrated the course of the recurrences on a living pig, tying them, releasing them, and finally cutting them. He compared the course of the recurrent nerves to that of a runner round a turning post. Through his metaphor they have come to bear the name *recurrent*.

For his experiments on the spinal cord I can do no better than repeat the words of the late W. G. Spencer:<sup>1</sup>

<sup>1</sup> W. G. Spencer, *Animal Experiments and Surgery*, Hunterian Lectures, London, 1920. By kind permission of the Royal College of Surgeons of England.

"Galen here employed monkeys, also young pigs in which he was able to cut through the spines and laminae with a strong knife. In monkeys he passed a fine, flat-bladed knife between the laminae, so as to cut across the cord transversely. To divide the spinal cord longitudinally, after removing spines and laminae, he raised the *dura mater* on a hook so as to incise it without wounding the *pia mater*. He then could cut the cord exactly along the middle line with a fine knife; there was no disturbance of function, neither the intercostal nerves nor the nerves to the hind limbs were paralysed.

"When the cord was divided transversely, the nerves connected with the spinal cord below the division lost the function both of sensation and of motion. If the section was at the level of the sacrum, sensation and motion were lost in the foot, and as the section was made higher up, so there was loss of sensation and of motion in the thigh, the hip and lumbar region. When the section was made at the level of the thoracic vertebrae, the forcible respiratory movements of the animal began to weaken. When the section was just below the middle of the dorsal region, movement continued in the upper intercostals, the upper accessory muscles of respiration and the diaphragm. Galen also noticed that the *Serratus posticus inferior* has a high nerve supply, an observation only confirmed in recent years.

"In monkeys, so long as the section was below the second intercostal space, power in the arms was preserved. A section just above this level caused loss of sensation in the skin of the axilla and inner side of the arms, i.e. in the distribution of the intercosto-humeral nerves. The hands of the monkey were weakened when the section was made at the level of the first rib. When the section was between the seventh and eighth cervical vertebrae, the forearms were weakened but the action of the accessory muscles of respiration continued. By a section at the level of the fifth cervical vertebra the arms were completely paralysed; the diaphragm continued in full movement, also the scaleni, whilst all the intercostal movement was lost."

Galen's career presents a unique phenomenon in the history of science and one perhaps unique in cultural history as a whole. Nearly every exhibition of human activity seems to go through a process of development, flowering, and decline. The Ancients, even the most scientific of them, were not generally great hands at experiment, and Galen represents the climax and flower of the experimental spirit in antiquity, certainly so far as the biological disciplines are concerned. He brought experimental physiology to a very high standard indeed, but he was quite without successors. There is no fading out of physiological activity. It simply disappears. Yet Galen was no solitary worker; he was constantly demonstrating his experiments to large audiences of colleagues and he had many pupils, but he had no followers or imitators. Ancient science fell dead with Galen.

Why was so triumphant a scientific career devoid of successors and even of imitators? This cannot be answered completely, but some inkling of the form that the answer will one day take may perhaps be reached by considering the intellectual associations of his age. The intellectual climate was certainly against experiment. The prevailing philosophy of the educated classes in Italy was Stoicism. This gave no warrant for or encouragement to the investigation of Nature. True, Galen's own thought was based on Stoicism, but he was neither an orthodox Stoic, nor had he the characteristic Stoic temper. The outlook of the Stoic was essentially fatalistic. It had developed a close alliance with the "astrology" of the time. In those days astrology was no idle superstition but a natural development of the ancient cosmology. It had crystallized into a rigid system of beliefs concerning the nature of events on our Globe under the mechanical working of the heavens that surrounded it. Man was enclosed within a spherical machine. Against it he could do nothing and all that he was and did and became was determined by it. There was a Supreme Power, but He was no pitying God nor would He control that pitiless machine. Perhaps God was the Spherical

Universe itself. Why then should man seek to know farther the minor details of that machine? Far better, in our earthly span, to turn to things of the mind. That is the temper of Marcus Aurelius. It is no mood for the investigation of Nature.

Epicureanism, the school of philosophy that was the great rival to Stoicism, was on the wane in Galen's time. It was no more friendly to the investigation of Nature. No investigator of antiquity is known to have professed the Epicurean creed. In practice Epicureanism was even more dogmatic on the unprovable structure of the universe than was Stoicism.

Putting aside the host of trivial cults, the third great competitor for the minds of men had also come, like the philosophies, from the East. As to whether the Christian faith was unfriendly to the investigation of Nature we need not discuss here. It certainly turned men's minds away from observation and away from experiment and fixed them on the inner world. Tertullian (c. 155-c. 222), the earliest of the Church writers of the West, besides studying as a youth in Rome, spent some five years there (c. 190-195) just at the time when Galen was at the height of his reputation. Tertullian had full command of Greek philosophical literature and from that he passed to the medical works and yet he makes no mention of Galen. As his thought developed he ceased to take any interest in the investigation of Nature except to oppose it. Dissection he despised and hated.

All the thought of the time was thus against Galen's experimental ways. But there was something within Galen as well as outside him that discouraged the further development of investigation. We have spoken of Galen as a modern but there is in him that which, rightly understood, would have closed the book of science for ever. It lies in certain of his philosophical assumptions. The point comes out best in his best known work *The uses of the parts of the human body*. There he seeks to show that the bodily organs are so well constructed and in such perfect relation to the functions to which they minister, that it is impossible to imagine anything better. Thus, following the Aristotelian principle that Nature makes naught in vain, Galen seeks to justify the form and structure of every organ, with reference to the functions for which he believes it is destined. We are thus in the presence of a work that is not, strictly speaking, on Anatomy and Physiology, but in which those sciences subserve a particular doctrine and are used to justify the ways of God to Man. We have, in fact, an extreme case of the thesis of Final Causes applied to the organism.

Galen thus holds that it is possible to discover the end served by each part which, being perfectly adapted thereto, could not be constructed other than as it is. To say this is to go even further than the *Bridgewater Treatises* which undertook, more than a hundred years ago, to demonstrate "the Power, Wisdom and Goodness of God as manifested in the Creation". It is to claim that in any work of Creation, and in every detail of such work, we can actually possess ourselves of knowledge which will enable us to demonstrate God's purpose. The acceptance of any such claim would involve cessation of all interest in investigation. Research would not be worth while because all of consequence that it could reveal would be already known. This was, in fact, the position of the early Church which did not deny the data of science but regarded them as irrelevant and trivial. Extremes had met. The teleology of Stoicism and the teleology of the rising faith of Christianity both turned men's eyes away from the material world. Galen was thus the last ancient as he was the first modern experimental physiologist.

## Section of Dermatology

President—J. E. M. WIGLEY, F.R.C.P.

[February 17, 1949]

**Lupus Vulgaris, Resistant to Calciferol. Treated with Streptomycin and Calciferol.**—R. M. B. MACKENNA, M.D., and BRIAN RUSSELL, M.D.

Mrs. G. C., aged 54. Two years' history of eruption on nose and cheeks. When first seen in February 1948 showed red, swollen nose and malar regions, with lymphatic obstruction and superimposed secondary infection. Ulceration of septum with early parrot-bill deformity. Stenosis of anterior nares. Profuse purulent nasal discharge.

With penicillin cream the condition improved, the swelling subsided, and nodules of lupus vulgaris became apparent.

*General health.*—Epileptic. Controlled by phenobarbitone and phenytoin.

*Past history.*—Eight years ago, erysipelas of face.

*Investigations.*—Wassermann and Kahn reactions negative. X-ray of chest, no abnormality. X-ray of antra, both opaque. Biopsy, typical appearances of lupus vulgaris.

*Treatment.*—From 6.10.48 was given vitamin D<sub>2</sub>, 150,000 units a day, with very little improvement; in December 1948, course of intramuscular penicillin injections and also alkaline nasal douches. From January 19, 1949, to February 8, she was given streptomycin intramuscularly, 1 gramme twice a day. Owing to painful reactions from the injections streptomycin was stopped for two days and then resumed in a dosage of 0.5 gramme, twice a day, on February 11, 1949. With this the patient's condition has greatly improved and the ulceration of the nostrils has almost cleared. Treatment with calciferol has been continued in the same dosage. Consideration was given, before streptomycin was administered, to the advisability of puncture and drainage of the infected antra, but one of the most marked features has been the lessening of the nasal discharge since streptomycin was begun.

For the last few days the patient has complained of heavy feelings in the head and instability when sitting up in bed.

We have presented this case because those who remember the *via dolorosa* of the patient with lupus vulgaris cannot fail to be impressed with this result of streptomycin treatment.



FIG. 1.—Taken on 29.9.48.



FIG. 2.—Taken on 10.2.49  
(i.e. three weeks after beginning  
treatment with streptomycin).



FIG. 3.—Taken on 1.4.49.

Dr. E. W. Prosser Thomas: This patient was previously under my care for about a year at another hospital, both as an out-patient and in-patient. She was given calciferol treatment but the lupus responded poorly, presumably because of the heavy infection and impetiginization in the nose, which was always most difficult to control. Her changed appearance today after combined calciferol and streptomycin treatment is very striking.

I have recently seen a case of multiple tuberculous sinuses which has responded dramatically to the same combination.

The following cases were also shown: Hirsuties, with Male Type Alopecia.—Dr. C. H. WHITTLE. Foreign Body Granuloma.—Dr. BERNARD GREEN. Case for Diagnosis.—Dr. L. A. MUSSO (introduced by Dr. J. E. M. WIGLEY). Acne Agminata.—Dr. H. T. H. WILSON. Disseminated Granuloma Annulare.—Dr. R. E. BOWERS. Monilethrix.—Dr. I. MARTIN-SCOTT. Dyshydrotic Cheilopompholyx.—Dr. IAN WHIMSTER. Tuberculoid Leprosy Under Treatment with Para-aminosalicylic Acid.—Dr. K. M. TOMLINSON.

Dr. I. A. Roxburgh read further notes on a case, shown to the Section in March 1948, and reported in the *Brit. J. Derm.* (1949) 61, 25, of a man with marked swelling of the lips and buccal mucosa due to acanthosis nigricans, and with signs of acromegaly.

(The above cases and report may be published later in the *British Journal of Dermatology*.)

[March 17, 1949]

**Werner's Syndrome.**—DAVID I. WILLIAMS, M.R.C.P.

B. L., aged 35, one-time hairdresser.

Werner (1904) described a syndrome of which nearly all the features are shown in this patient. There is usually shortness of stature, canities, premature alopecia, what Werner called "sclero-poikiloderma", trophic ulcers of the legs, hypogonadism, a tendency to diabetes, calcification of blood vessels, metastatic calcification, osteoporosis, juvenile cataracts and a tendency for the condition to occur in brothers and sisters. In the present case there are also clinical and histological changes in certain muscles.

**History.**—In May 1948 he reported to the Orthopaedic Department of King's College Hospital complaining of stiff feet. He was referred to the Skin Department. The legs have always been weak; the feet burn if he stands all day. The skin of the legs has always been fragile and since 1944 has been getting paler. Ulcers on the left heel and the right leg have recently developed following minor trauma. He cannot remember when he began to lose his toe-nails. His eyesight began to fail at the age of 8 and cataracts have been needled on several occasions since the age of 22. His wrists have been getting stiff recently. He shaves at most twice a week. His hair has been getting thin on top.

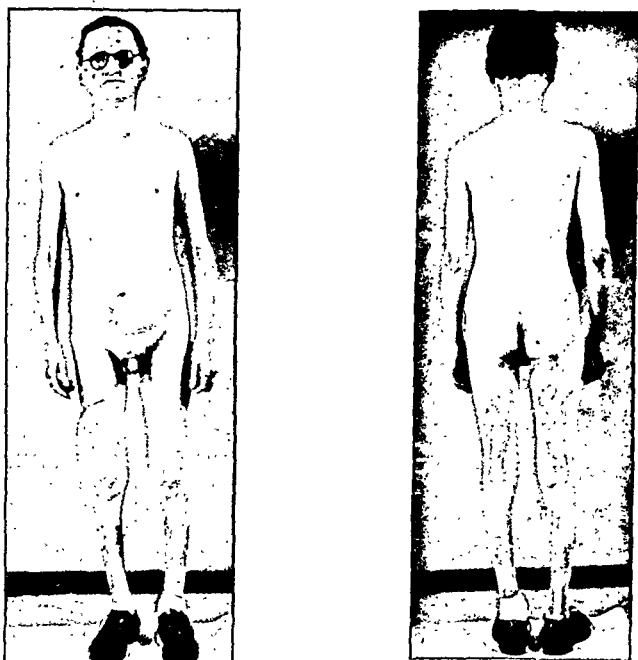


FIG. 1.—Werner's syndrome.

**Family history.**—His parents, who were first cousins, came from Odessa. He has two sisters. Nobody else in the family is similarly afflicted.

**On examination.**—The patient is thin and obviously undersized, weighing only 6 st. His intelligence is reasonable. The voice is high pitched but there is no laryngeal abnormality. The testicles are very small. His arms are thin and power is only fair. Limitation of movement of the wrists was present in May 1948 but has improved markedly with nine months' physiotherapy. The skin of the legs is pale, thin and tightly stretched over the joints. There are telangiectasia and macular pigmentation of the legs and many small waxy papules. There is an indolent ulcer over the right external malleolus. The toe-nails are dystrophic or lost. There is scarring around the knees reminiscent of that seen in cases of epidermolysis bullosa. The leg muscles feel hard. Movement of the ankles is negligible. Scalp hair is scanty and greying; body hair is also sparse. He is aphakic.



**Investigations.**—B.P. 190/100. Urine: No sugar, no acetone. Glucose tolerance: A slightly raised peak and delayed return to the fasting level. Blood-count: Normal. Serum calcium: 10.4 mg./100 ml.

A forty-eight-hour specimen of urine produced maximum stimulation of rat uterus and ovaries with six-hour and twelve-hour aliquots (i.e. above normal limits).

Twenty-four-hour specimen of urine: 17-ketosteroids 10 mg./24 hour. This is within normal limits for the male but a high proportion of dehydroisoandrosterone suggests that the source is mainly adrenal. These findings indicate a primary gonadal failure.

Electrocardiogram normal. Electromyograph: The anterior tibials and calf muscles of both legs showed greatly reduced action potentials. Electrical reactions normal.

X-rays: The bones of the legs and feet are generally porotic with coarse trabeculation and thinned cortices. A cystic lesion is present in the head of the left tibia. The feet are short with mal-developed terminal phalanges. Flakes of calcification are seen alongside the tarsal bones and there is some calcification of the arteries of the legs. *Sella turcica* normal.

**Histology** (Professor H. A. MAGNUS).—Section of the skin shows the epidermis to be atrophic. There is possibly some increase in the amount of collagenous tissue present in the corium but this is not a striking feature. Some of the smaller arteries in the subcutaneous tissue show a moderate amount of obliterative endarteritis. Section of the muscle shows the fibres to be swollen and many have lost their striations. In some areas the fibres have completely disappeared and been replaced by fibrous tissue. There is no cellular infiltration of the interstitial tissue. Again some of the smaller arteries show a considerable degree of obliterative endarteritis.

The leg ulcer has proved quite intractable and suggestions as to how to heal it would be welcomed. I should be glad to hear from the histology experts what they think of the muscle changes. There has been discussion in time past as to whether true scleroderma occurs in this syndrome: the skin changes in this case together with the muscle anomalies confuse the issue still further.

#### REFERENCES

- WERNER, C. W. O. (1904) Über Katarakt in Verbindung mit Sclerodermie. Inaug. Dissert. Kiel.  
THANNHAUSER, S. J. (1945) *Ann. intern. Med.*, 23, 559.

**Dermatitis Herpetiformis with Ocular Manifestations.**—P. J. HARE, M.B., for W. N. GOLDSMITH, M.D.

R. T., aged 61, widow.

**History.**—In July 1947 frequent nose-bleeding began and a constant mucopurulent nasal discharge. Six months later blisters appeared in the mouth, followed shortly by a few blisters on the trunk and limbs, with violent itching. The skin eruption cleared but recurred on successive occasions; the mucosal lesions appear to have persisted throughout. Finally, about July 1948, pain in the eyes began, with photophobia and blepharospasm. The eye condition has become steadily worse until now the patient is nearly blind.

Admitted to University College Hospital on 11.1.49, from Moorfields, with a diagnosis of pemphigus.

**Past history.**—No previous skin disorders. Deaf in both ears for fifteen years. No habitual drugs.

**Family history.**—Nothing relevant.

**Examination on admission.**—An obese woman, completely edentulous, very deaf and almost completely blind. General examination revealed nothing abnormal. B. P. 140/85.

**Skin:** A few scattered lesions on the back and limbs, but mainly localized to the mid-chest in front, beneath the pendulous breasts and in the axillæ: erythematous areas 1 cm. across, vesicles 2-3 mm. across, not strikingly grouped, with irregular outlines and cloudy contents. Some vesicles have an erythematous halo of 1 cm. diameter; others arise from apparently normal skin. There are also excoriations, bloodscabs and reddish-brown pigmented areas.

**Mouth:** Tense vesicles with red haloes on the mucosa of palate, fauces and cheeks.

**Nose:** Similar vesicles on the mucosa of both nostrils, involving floor, septum and turbinates.

**Vagina:** No lesions seen.

**Eyes:** Obliteration of conjunctival fornices and partial symblepharon. Ulceration, opacity and partial fibrous obliteration of the corneæ. Vision: light-perception only.

**Ears:** No lesions in external canals. Conduction deafness.

**Investigations.**—**Vesicle fluid:** sterile on culture. No cells seen. **Blood:** Hb 82%, W.B.C. 7,200 (polys. 69%, lymphos. 22%, monos. 5%, basos. 2%, eosinos. 2%). Urine: acid, no sugar or albumin, deposit normal.

**Skigrams:** Sinuses: slight thickening of antral mucosæ. Jaws: tooth fragment in upper jaw; no sepsis. Chest normal.

Iodide test: Oral test not performed. Patch-test with 20% potassium iodide in soft paraffin caused erythema and vesiculation in twenty-four hours.

**Histology.**—Sections show a subepidermal bulla containing fibrin and numerous eosinophils and lymphocytes. There is œdema of the corium and a perivascular infiltrate of round cells and eosinophils.

**Treatment.**—Sulphapyridine 2 grammes initially, 1 gramme 4-hourly, 7 days; 0.5 gramme 6-hourly, 7 days; 0.5 gramme 8-hourly, 19 days. Liq. arsenicalis 4 minims t.i.d. thereafter.

**Course:** The skin lesions cleared after two weeks' treatment with sulphapyridine. Some pruritus remains. The mucosal lesions persist but are perhaps a little improved since the exhibition of arsenic. Vision is deteriorating. General condition stationary.

**Summary.**—An Englishwoman, aged 61, with a two years' history of successive disease of the nose, mouth, skin and eyes. The case is presented as one of dermatitis herpetiformis: this diagnosis is suggested by the length of history, without marked impairment of the general health, by the remittent course, the severe pruritus, the small size of lesions and their polymorphic character, the sensitivity to iodide and the response to treatment.

Ocular pemphigus, whilst rare, must be commoner than dermatitis herpetiformis of the eye. Dühring does not mention this complication of dermatitis herpetiformis. (Macleod in the 1915 discussion here (*Proc. R. Soc. Med.*, 8, Sect. Derm., 174) commented on its rarity and Sir Malcolm Morris said he had never seen an example of it.) Riecke in Jadassohn's *Handbuch* (1931; VII/2, 578) devotes a short paragraph to the ocular manifestations of dermatitis herpetiformis, enumerating reported cases and the lesions encountered, and concluding that the latter are similar to those of pemphigus and that it is doubtful if they can be separated.

Points of particular interest in this case are the history of the appearance of mucosal lesions well before involvement of the skin, their persistence and lack of response to treatment, in contrast to the rapid clearance of the skin lesions by sulphapyridine. Such a case may be considered to support the relationship of pemphigus and dermatitis herpetiformis.

**Dr. J. Sommerville:** This is an interesting case. For some time I have thought there could be a relationship between pemphigus and dermatitis herpetiformis. I recall particularly an acute case where the picture changed quite irregularly from pruritus to absence of pruritus and from "herpetiformis" in an extensive way to pemphigus in an extensive way. The patient ultimately died from pemphigus. The present case shows a connexion between pemphigus and dermatitis herpetiformis.

**Dr. B. C. Tate:** I agree that this case shows the gradation from one to the other. Everybody has probably seen similar cases of pemphigus starting as classical dermatitis herpetiformis. I remember one which was diagnosed in 1926 as dermatitis herpetiformis; I followed the man up for ten years and in the end one could not have found a better textbook picture of pemphigus vulgaris. Pemphigus foliaceus should come into the same group, and the Seneac-Usher type of pemphigus is the same.

**Dr. Brian Russell:** When I saw this patient some months ago I formed the opinion that the condition was pemphigus and so was pleasantly surprised to find that on that occasion also there was a good response to sulphapyridine. Two years ago, I saw a patient who seemed to have typical pemphigus vegetans and who also responded very well temporarily to sulphapyridine.

**Dr. H. R. Vickers:** The patch test with potassium iodide is still being used to try to differentiate between the two conditions. At a recent meeting I showed two cases with typical pemphigus both of whom gave a strongly positive patch test. My own view is that potassium iodide patch-testing is quite useless to make a diagnostic differentiation, if these really are two different conditions. I would mention a case being looked after by my colleague, Dr. I. B. Sneddon, of pemphigus of the eyes, not so severe as this case, which is being controlled by injections of suramin and I wondered if it would be worth while trying suramin on this patient.

**Dr. G. B. Dowling:** Cytodiagnosis carried out at St. Thomas's Hospital according to the technique advocated principally by Tzanck has so far proved reliable in distinguishing a few cases of pemphigus from other bullous conditions such as dermatitis herpetiformis, erythema multiforme and certain drug eruptions.

**Dr. H. J. Wallace:** I have been asked by Dr. Dobkevich, from Dr. Civatte's Laboratory, to state that she considers the section characteristic of dermatitis herpetiformis.

**Dr. W. N. Goldsmith:** The differentiation of dermatitis herpetiformis and pemphigus by cyto-diagnosis rests on the kind of cells one detaches from the floor of a blister. Would not its validity then be upset if Professor Percival is right in his opinion (PERCIVAL and HANNAY, 1949, *Brit. J. Derm.*, 61, 41 and 77) that the blisters of both these diseases originate between dermis and epidermis?

**Dr. Ian Whimster:** The site of origin of the bullæ in these two conditions, though a matter of great interest and probably of importance, has little direct bearing on Tzanck's cytodagnostic test. As Percival and Hannay have shown the majority of the bullæ in both conditions have their floors at any rate partially covered by epithelium and a scraping from the floor of a bulla in either condition will thus usually contain some epithelial cells. Tzanck's test depends on the microscopic appearances of these cells when appropriately fixed and stained and not on the mere presence or absence of epithelial elements in the smear.

The following cases were also shown: **Necrobiosis Lipoidica (Non-Diabetic).**—Dr. BENTLEY PHILLIPS. **Urticaria Pigmentosa in an Adult.**—Dr. E. W. PROSSER THOMAS and Dr. A. J. ROOK. **Morbus Hansenii (Tuberculoid Type).**—Dr. BRIAN RUSSELL. **Leprosy.**—Dr. S. P. HALL-SMITH. (These cases may be published later in the *British Journal of Dermatology*.)

## Section of Physical Medicine

President—L. C. HILL, M.D., F.R.C.P.

[February 9, 1949]

### DISCUSSION ON NEUROLOGICAL ASPECTS OF RHEUMATIC DISEASES

**Dr. H. Lovell Hoffman:** *Nerve Root Involvement in Vertebral Arthritis [Abridged].*

I intend briefly to consider nerve root involvement in vertebral arthritis. It may occur in all three varieties, namely osteoarthritis, ankylosing spondylitis and rheumatoid arthritis, but is far more common in osteoarthritis which I will discuss first.

*Spinal osteoarthritis.*—Since the recognition of the syndrome of the prolapsed intervertebral disc, much less attention has been paid to spinal osteoarthritis as a cause of brachial pain and sciatica. Some authorities deny that they can be so caused, and, in the absence of any other lesion, tend to ascribe these symptoms to disc prolapse. Others like Nachlas (1944) and Buckley (1945) agree that osteoarthritis can produce nerve root damage, and in November 1947 Russell Brain described the syndrome in a discussion of brachial neuralgia at a meeting of this Section. I am personally convinced that root compression in elderly persons is very commonly due to osteoarthritis.

As this is a clinical paper, I do not wish to enter too deeply into speculation regarding the morbid anatomy of the syndrome in question. Briefly, it may be said that the intervertebral discs begin to degenerate after the fourth decade, and from this time onwards true herniation of the nucleus pulposus becomes less and less common. Bradford and Spurling (1941) state that only occasional cases are found in the seventh and eighth decades. This degeneration, consequent shrinkage, and loss of elasticity of the discs has several results (fig. 1A and B). The intervertebral disc spaces are

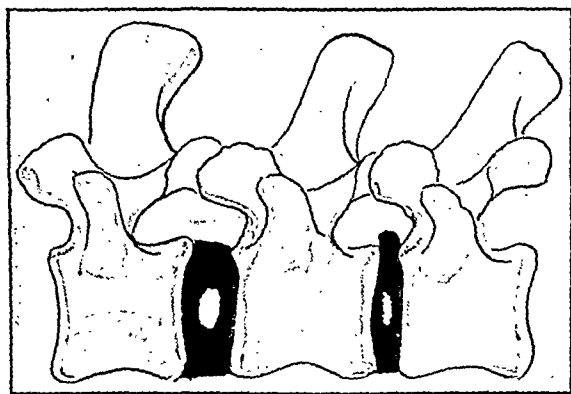


FIG. 1A.

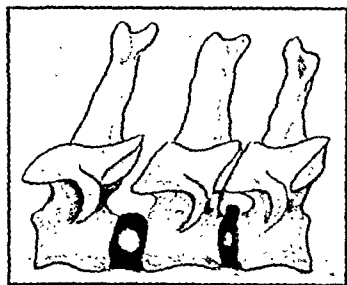


FIG. 1B.

FIG. 1 A and B.—Drawings of (A) lumbar, and (B) cervical vertebrae, showing the effects of degeneration and shrinkage of the intervertebral discs as described in the text.

reduced in size and therefore the intervertebral foramina are narrowed in their vertical diameters (Brain, 1948). The annulus fibrosus is pressed back and protrudes into the spinal canal, reducing the size of the foramina from before backwards. It should be remembered, however, that this protrusion of the annulus of the disc is merely part of the pathology of spinal osteoarthritis, and very different from the florid prolapse of the turgid nucleus pulposus of younger persons. Finally, narrowing

Iodide test: Oral test not performed. Patch-test with 20% potassium iodide in soft paraffin caused erythema and vesiculation in twenty-four hours.

**Histology.**—Sections show a subepidermal bulla containing fibrin and numerous eosinophils and lymphocytes. There is œdema of the corium and a perivascular infiltrate of round cells and eosinophils.

**Treatment.**—Sulphapyridine 2 grammes initially, 1 gramme 4-hourly, 7 days; 0.5 gramme 6-hourly, 7 days; 0.5 gramme 8-hourly, 19 days. Liq. arsenicalis 4 minims t.i.d. thereafter.

**Course:** The skin lesions cleared after two weeks' treatment with sulphapyridine. Some pruritus remains. The mucosal lesions persist but are perhaps a little improved since the exhibition of arsenic. Vision is deteriorating. General condition stationary.

**Summary.**—An Englishwoman, aged 61, with a two years' history of successive disease of the nose, mouth, skin and eyes. The case is presented as one of dermatitis herpetiformis: this diagnosis is suggested by the length of history, without marked impairment of the general health, by the remittent course, the severe pruritus, the small size of lesions and their polymorphic character, the sensitivity to iodide and the response to treatment.

Ocular pemphigus, whilst rare, must be commoner than dermatitis herpetiformis of the eye. Duhring does not mention this complication of dermatitis herpetiformis. (Macleod in the 1915 discussion here (*Proc. R. Soc. Med.*, 8, Sect. Derm., 174) commented on its rarity and Sir Malcolm Morris said he had never seen an example of it.) Riecke in Jadassohn's Handbuch (1931; VII/2, 578) devotes a short paragraph to the ocular manifestations of dermatitis herpetiformis, enumerating reported cases and the lesions encountered, and concluding that the latter are similar to those of pemphigus and that it is doubtful if they can be separated.

Points of particular interest in this case are the history of the appearance of mucosal lesions well before involvement of the skin, their persistence and lack of response to treatment, in contrast to the rapid clearance of the skin lesions by sulphapyridine. Such a case may be considered to support the relationship of pemphigus and dermatitis herpetiformis.

**Dr. J. Sommerville:** This is an interesting case. For some time I have thought there could be a relationship between pemphigus and dermatitis herpetiformis. I recall particularly an acute case where the picture changed quite irregularly from pruritus to absence of pruritus and from "herpetiformis" in an extensive way to pemphigus in an extensive way. The patient ultimately died from pemphigus. The present case shows a connexion between pemphigus and dermatitis herpetiformis.

**Dr. B. C. Tate:** I agree that this case shows the gradation from one to the other. Everybody has probably seen similar cases of pemphigus starting as classical dermatitis herpetiformis. I remember one which was diagnosed in 1926 as dermatitis herpetiformis; I followed the man up for ten years and in the end one could not have found a better textbook picture of pemphigus vulgaris. Pemphigus foliaceus should come into the same group, and the Seneac-Usher type of pemphigus is the same.

**Dr. Brian Russell:** When I saw this patient some months ago I formed the opinion that the condition was pemphigus and so was pleasantly surprised to find that on that occasion also there was a good response to sulphapyridine. Two years ago, I saw a patient who seemed to have typical pemphigus vegetans and who also responded very well temporarily to sulphapyridine.

**Dr. H. R. Vickers:** The patch test with potassium iodide is still being used to try to differentiate between the two conditions. At a recent meeting I showed two cases with typical pemphigus both of whom gave a strongly positive patch test. My own view is that potassium iodide patch-testing is quite useless to make a diagnostic differentiation, if these really are two different conditions. I would mention a case being looked after by my colleague, Dr. I. B. Sneddon, of pemphigus of the eyes, not so severe as this case, which is being controlled by injections of suramin and I wondered if it would be worth while trying suramin on this patient.

**Dr. G. B. Dowling:** Cytodiagnosis carried out at St. Thomas's Hospital according to the technique advocated principally by Tzanck has so far proved reliable in distinguishing a few cases of pemphigus from other bullous conditions such as dermatitis herpetiformis, erythema multiforme and certain drug eruptions.

**Dr. H. J. Wallace:** I have been asked by Dr. Dobkevich, from Dr. Civatte's Laboratory, to state that she considers the section characteristic of dermatitis herpetiformis.

**Dr. W. N. Goldsmith:** The differentiation of dermatitis herpetiformis and pemphigus by cyto-diagnosis rests on the kind of cells one detaches from the floor of a blister. Would not its validity then be upset if Professor Percival is right in his opinion (PERCIVAL and HANNAY, 1949, *Brit. J. Derm.*, 61, 41 and 77) that the blisters of both these diseases originate between dermis and epidermis?

**Dr. Ian Whimster:** The site of origin of the bullæ in these two conditions, though a matter of great interest and probably of importance, has little direct bearing on Tzanck's cyto-diagnostic test. As Percival and Hannay have shown the majority of the bullæ in both conditions have their floors at any rate partially covered by epithelium and a scraping from the floor of a bulla in either condition will thus usually contain some epithelial cells. Tzanck's test depends on the microscopic appearances of these cells when appropriately fixed and stained and not on the mere presence or absence of epithelial elements in the smear.

The following cases were also shown: Necrobiosis Lipoidica (Non-Diabetic).—Dr. BENTLEY PHILLIPS. Urticaria Pigmentosa in an Adult.—Dr. E. W. PROSSER THOMAS and Dr. A. J. ROOK. Morbus Hansenii (Tuberculoid Type).—Dr. BRIAN RUSSELL. Leprosy.—Dr. S. P. HALL-SMITH. (These cases may be published later in the *British Journal of Dermatology*.)

Single herniations of the nucleus pulposus being rare after the age of 60, multiple protrusions must be rarer still. If, therefore, in an elderly person, we find the symptom of sciatica or brachial neuralgia, in which several roots are involved, X-rays show osteoarthritis—and other causes have been excluded—we can be practically certain that the arthritis is the cause of the symptoms. Any of the signs of root involvement may be present in greater or less degree. Thus we may see well-marked muscle wasting, sensory loss, and diminution of reflexes. Fibrillation, though rare, does occur occasionally. The following case is fairly typical.

CASE I.—J. M., male, aged 54. Charcoal burner. First examined on 26.11.46.

During the period April 1945 to April 1948, he complained at various times of the following symptoms: Pain in the lower back, outer L. thigh, calf, and inner L. foot with paræsthesiæ. Pain in the outer R. thigh. Pain from the neck, to the second and third digits of the R. hand.

*Physical signs.*—Neck movements limited. Flattening of lumbar spine, with alternating scoliosis. Flexion, and flexion to left limited. Straight leg raising R. 80 degrees; L. 70 degrees. Ankle sign positive. Neck and Naffziger's sign negative. L. ankle-jerk at first absent, returned later. R. ankle-jerk at first present, but disappeared later. Weakness of R. triceps. Hypalgesia of second and third digits of R. hand, of the inner side of the L. foot, and the outer side of the R. foot. Fibrillation of R. buttock and posterior thigh. C.S.F. normal. X-rays: see fig. 2.

*Treatment.*—Exercises for lumbar spine in the deep pool, and later a spinal brace. The sciatica improved. Manipulation of the cervical spine. Neck exercises, massage with neck traction. The pain in the hand diminished, and in May 1948 the hypalgesia only involved the third digit.

Cases of this sort are excellent evidence of the existence of the syndrome in question. In this patient there was involvement of at least three spinal roots, namely L.5 on the left and C.7 and S.1 on the right. The brachial pain was relieved by active manipulation of the neck, which was suitable for osteoarthritis, but which would have been dangerous, or at least would have aggravated the symptoms in a case of prolapsed nucleus pulposus. If only one root is involved, it is much more difficult to exclude this condition. In the lumbar region it usually produces a flattened or slightly kyphotic spine, in which flexion is limited, but lateral flexion is relatively free. In osteoarthritis, on the other hand, there may be very marked lordosis, and all spinal movements are equally limited. The C.S.F. is more likely to show an increase of protein in cases of prolapsed nucleus pulposus, but it is possible that the protrusion of the annulus described above in osteoarthritis may also cause a slight increase. Cord and long tract signs will be found in cases of spinal or vertebral neoplasm, or sometimes in disc lesions of the cervical region. They never occur in osteoarthritis. The symptoms of new growth progress relentlessly, whereas those of osteoarthritis are variable and may clear up either when the swelling in the posterior intervertebral joints has subsided, or when these joints become fixed. It sometimes improves with movement as the day wears on. The middle-aged patient, his head supported by pillows, terrified to move his neck, who cries out in pain when the bed is accidentally jarred, almost certainly has secondary new growth in his cervical vertebræ. In differential diagnosis the blood sedimentation rate is helpful, being very rapid in secondary bone neoplasm and normal in osteoarthritis.

*Ankylosing spondylitis.*—Although girdle pains, and pains in the limbs suggestive of root distribution, occur in ankylosing spondylitis, it is uncommon to find objective signs of root compression. Burt in 1933 considered that this was due to the fact that early immobilization occurred in this condition. Sciatica is sometimes the first symptom of ankylosing spondylitis. Of 200 cases reviewed at the Royal National Hospital for Rheumatic Diseases by Simpson and Stevenson (1949) 12 were found to have complained of this symptom. It is sometimes considered that the sciatic pain is referred from the sacro-iliac joint which is so often involved early in the disease. If, however, there are paræsthesiæ, sensory loss, muscle weakness or diminution of the knee or ankle-jerk, root compression in the lumbosacral region must be held responsible. The following case of ankylosing spondylitis is somewhat atypical, but showed definite evidence of root damage.

of the disc space and loss of elasticity of the disc throw extra strain on the posterior intervertebral joints, and bring their articular surfaces into closer apposition, perhaps at a different angle. This occurs especially in parts of the spine where there is a natural lordosis, namely the mid-cervical and lumbar regions, as pointed out by Shore (1935). It is not difficult to imagine osteoarthritis occurring in these joints in such circumstances, and if small effusions occur as a result of cold, damp, and minor trauma, the intervertebral foramina will be narrowed still further, this time from behind forwards. This narrowing of the intervertebral foramina in all their diameters, leaves considerably less room for the spinal nerve roots which pass through them, and it is easy to see how these roots may be compressed or irritated. It is probable, however, that this compression and irritation are due to soft tissue, or to the joint effusions, rather than to actual osteophytic formation. Fig. 2 shows an oblique

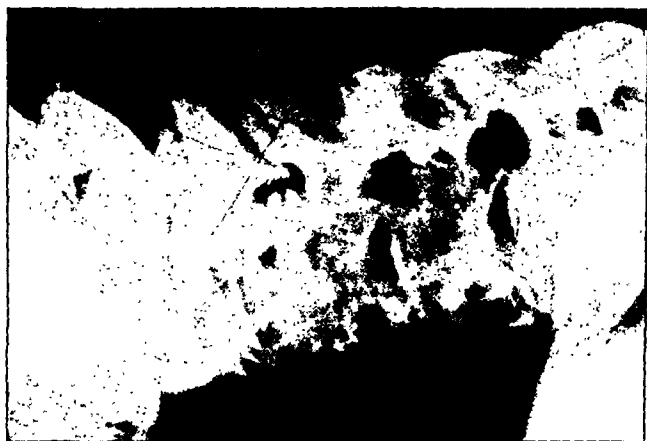


FIG. 2.—Oblique X-ray of the cervical spine of Case I, showing narrowing of the foramina for the sixth and seventh cervical roots. Osteophytes on the posterior aspect of the vertebral bodies are seen encroaching on these foramina.

X-ray view of the cervical spine, in which the foramina of the sixth and seventh cervical roots are especially narrowed, and posterior lipping is seen in the bodies of the affected vertebrae. Although X-rays are helpful in differential diagnosis, it must be remembered that cases of prolapsed nucleus pulposus often show the changes of osteoarthritis, whereas osteoarthritis may cause symptoms when only minimal X-ray changes are present. Sometimes damaged nerve roots are found emerging from that part of the spine which is most mobile, and which shows least evidence of osteoarthritis on X-ray. This may be explained by assuming that effusions are more likely to occur in semi-mobile joints than in those which have become fixed. It seems likely that some degree of movement is necessary for the production of root damage.

Putti (1927) believed that most cases of sciatica were caused by arthritis of the posterior intervertebral articulations, but many of his cases would now be considered to be due to prolapse of the nucleus pulposus. In 100 cases of sciatica which I have collected in the past three years, 13 showed signs of a root lesion which was thought to be due to osteoarthritis. In the same series there were 15 cases of disc prolapse proved by operation, and 29 treated conservatively, where the diagnosis was made on clinical grounds—in all a total of 44 cases. Bull (1948), in his paper to the Neurological Section, drew attention to the joints of Lushka situated at the posterolateral borders of the cervical vertebrae. He described the manner in which nerve roots could be compressed between these joints and the posterior intervertebral joints, should small effusions occur.

## BIBLIOGRAPHY

- BRADFORD, F. K., and SPURLING, R. G. (1941) *The Intervertebral Disc*. Baltimore.  
 BRAIN, W. R. (1948) *Lancet* (i), 393.  
 BUCKLEY, C. W. (1945) *Ann. rheum. Dis.*, 4, 54.  
 BULL, J. W. D. (1948) *Proc. R. Soc. Med.*, 41, 513.  
 BURT, J. BARNES (1933) *Proc. R. Soc. Med.*, 26, 1396.  
 NACHLAS, I. W. (1944) *J. Bone Jt. Surg.*, 26, 177.  
 PUTTI, V. (1927) *Lancet* (ii), 53.  
 SHORE, L. R. (1935) *Brit. J. Surg.*, 22, 833.  
 SIMPSON, N. R. W., and STEVENSON, C. J. (1949) *Brit. med. J.* (i), 214.

**Dr. F. A. Elliott:** *The Neurological Manifestations of the Rheumatic Diseases.*

In my view, the nervous system is implicated in only two forms of rheumatic disease—the chorea of acute rheumatic infection, and the root compression syndromes of spinal osteoarthritis. In the latter, narrowing of the intervertebral foramina by disc protrusions may play a part, but the occurrence of pain and sensory loss in the distribution of the second cervical root, associated with cervical arthritis, indicates that some other factor is operative since there is no disc between the atlas and the axis. This factor is probably inflammation of the dural root sheaths, which are often found to be thickened, fibrosed, and adherent to the small joints of Lushka which—as Bull (1949) has pointed out—are situated immediately in front of the emerging roots and are always involved in spinal osteoarthritis. Spread of an inflammatory process to the roots from the main intervertebral joints is rendered unlikely by the interposition of the thick ligamentum subflavum.

There is still doubt as to whether there is such a thing as a primary interstitial neuritis of rheumatic origin. Renton (1907) and Pers (quoted by Grundmann, 1926) have reported thickening, redness, and perineural adhesions of the sciatic nerve in a joint total of 79 cases of sciatica operated upon for “nerve stretching”, yet Hunt (1905), Thomas (1905) and Denny-Brown (1933) failed to find histological evidence of gross inflammation in their autopsy material. While it is certain that most of the cases of sciatic, femoral, and brachial “neuritis” of former days were due to disc lesions, the facts do not yet warrant summary rejection of interstitial neuritis as a pathological and clinical entity.

I now want to report some personal observations on the responses of intramuscular arteries to painful stimuli, because they would appear to be relevant to the vexatious problem of muscular atrophy occurring in relationship to painful joints. This investigation was initiated because of a growing curiosity as to why some patients with sciatica present objective coldness of the affected foot. This is an old observation, and Roger (1930) reported that in some cases there was a reduction of arterial pulsation in the calf as judged by the oscillometer. Disuse of the painful limb is doubtless partly responsible for this state of affairs, but another possibility, viz. active vasoconstriction in response to pain, was suggested by a personal case:

A man aged 42, suffering from severe sciatica, was found to have the signs of a herniation of the fourth lumbar disc with implication of the fifth lumbar root. This was subsequently verified at operation. But in addition to the neurological features, he was found to have no pulsation in the dorsalis pedis or posterior tibial artery in the affected side, pulsation in the unaffected leg being normal. After three hours' rest in bed the pulsation returned, but it again disappeared temporarily after a two-mile walk which brought on an exacerbation of his sciatic pain. There was  $\frac{3}{4}$  in. of wasting in the circumference of the leg below the knee. There was no evidence of cardiovascular disease.

Although the vascular phenomena displayed by this man were unusual, the question arose whether similar changes, though of less severity, occurred in other cases of radicular sciatica, and, further, whether the deep vessels to the muscles were affected in the same way as the arteries at the ankle. The oscillometer could not give an accurate answer to either question, so it was decided to investigate muscle temperatures directly by thermo-electric methods. The temperature of any tissue is determined by (a) its depth from the surface, (b) the temperature of the surroundings,

CASE II.—Mrs. K. W., aged 36.

1941: Right-sided sciatica.

November 1945: Backache after birth of third child. Pain and weakness in R. leg. Operation for prolapsed disc considered.

March 1946: Sudden loss of use of the right arm with partial recovery. Numbness in second to fifth digits. Stiffness in neck and pain in upper dorsal spine. Considerable loss of weight.

*On examination.*—There was pain and limitation of movement in the whole spine. The stance and appearance were typical of ankylosing spondylitis; there was weakness of the right triceps and hypalgesia over the first three digits of the right hand. There was also a persistent area of hypalgesia over the outer side of the right foot.

X-ray of the sacro-iliac joints and lower lumbar region showed changes of ankylosing spondylitis, but the rest of the spine was normal. The sedimentation rate was rapid. This patient was given a plaster bed and deep X-ray treatment to the cervical spine and sacro-iliac joints. Subsequently there was an attack of iritis, but the disease became arrested and the patient gained over a stone in weight. When last seen early in January 1949 she was well except for some slight right-sided sciatica and tingling in the digits of the L. hand where some hypalgesia was found.

*Rheumatoid arthritis.*—In this condition nerve-root compression is still more common. It may be seen in the following circumstances: (1) Where the posterior intervertebral joints and the joints of Lushka are involved in the rheumatoid process and there is effusion therein. (2) When these joints are affected by secondary osteoarthritis. (3) In very rare and severe cases where there is actual collapse of the vertebræ. The following case is an example of this:



FIG. 3.—Longitudinal section of the cervical spine of Case III, showing collapse of vertebræ due to the changes of rheumatoid arthritis. The cord is compressed.

CASE III.—R. T., male, aged 48.

The patient was under the care of Dr. L. C. Hill who has kindly allowed me to quote the case. I personally saw the patient very briefly while he was in hospital.

In 1937 he developed typical rheumatoid arthritis and a year later was unable to walk. He was admitted many times to the Royal National Hospital for Rheumatic Diseases, the final occasion being in September 1945. In October he developed severe pain in the neck and an X-ray showed collapse of the third and fourth cervical vertebræ. In December 1945 there was a spontaneous fracture dislocation of the right shoulder, and, not unnaturally, the clinical diagnosis was made of secondary new growth in the bones.

In March 1946 he developed paræsthesiæ in the arms and hypalgesia of C.6 and 7 root distribution. There was also a spastic paresis of the legs with ankle clonus, and a positive Oppenheim's sign on the left. He did not die until June 1946. Post-mortem examination revealed no evidence of new growth, the bone changes being those associated with rheumatoid arthritis (fig. 3).



difference in the deep temperatures of the two legs. In the remaining 10, the muscles supplied by the sciatic nerve in the painful limb were cooler than the corresponding muscles of the opposite side. But the quadriceps was unaffected, so the fall of temperature could not be attributed to disuse of the limb as a whole. The temporary vasoconstriction noticed clinically in the case quoted above suggested that the same explanation might account for the low temperatures in these cases, so a spinal anæsthetic was given to Cases 13 and 14, temperature recordings being done before and during anæsthesia (Table III). The temperature of both legs rose, but the rise

TABLE III.—SHOWING THE REVERSAL OF THE TEMPERATURE DIFFERENCES IN THE SCIATIC MUSCLES UNDER SPINAL ANÆSTHESIA. EXPRESSED IN FRACTION OF A DEGREE CENTIGRADE.

|         | Muscle         | Before spinal | During spinal |
|---------|----------------|---------------|---------------|
| Case 13 | Quadriceps ..  | — .15         | + .2          |
|         | Biceps fem. .. | — .3          | equal         |
|         | Tib. ant. ..   | — .2          | + .2          |
|         | Gastrocnem. .. | — .7          | + .25         |
| Case 14 | Quadriceps ..  | + .2          | equal         |
|         | Biceps fem. .. | — .4          | + .2          |
|         | Tib. ant. ..   | — .3          | equal         |
|         | Gastrocnem. .. | — 1.0         | + .1          |

was greater in the muscles of the affected side, which now became warmer than those of the opposite leg. This observation gives strong support to the view that reflex vasoconstriction had been present, and that it was greater in the painful leg than in the normal limb.

Reflex vasoconstriction of superficial vessels in response to pain has been demonstrated by Doupe *et al.* (1937) and by Travell and her associates (1944), who showed that a single, unilateral painful stimulus gave rise to transient bilateral vasoconstriction. The persistent, localized response found in the present work is a very different matter, but the two sets of observations are scarcely comparable.

We cannot assume that superficial vessels and deep vessels behave in the same fashion. Moreover, the persistent pain from an irritative root lesion is very different from a single painful stimulus applied to the skin under experimental conditions.

Does persistent vasoconstriction of this order give rise to muscular atrophy? The presence of a root lesion vitiates any attempt to correlate atrophy and ischæmia in the cases under discussion, and the problem remains unsettled. This technique has been applied to a few cases of rheumatoid arthritis and has shown a reduction of temperature in muscles related to the painful joints, but the all-important effect of sympathetic block has yet to be investigated. These preliminary observations are mentioned here in the hope that those interested in the rheumatic diseases will take up what appears to be a promising method of investigation.

#### REFERENCES

- BULL, J. W. D. (1949) *Brit. J. Radiol.*, 22, 68.  
 DENNY-BROWN (1933) *Proc. R. Soc. Med.*, 26, 1399.  
 DOUPE, J., ROBERTSON, J. S., and CARMICHAEL, E. A. (1937) *Brain*, 60, 281.  
 GRUNDMANN, H. (1926) *Med. Klin.*, 22, 1454.  
 HUNT, R. (1905) *Amer. Med.*, 9, 620.  
 RENTON, P. (1907-08) *Proc. R. Soc. Med.*, 1, 167.  
 ROGER, H. (1930) *Rev. Neurol.*, 17, 1032.  
 THOMAS A. (1905) *Rev. Neurol.*, 13, 139.  
 TRAVELL, J., BERRY, C., and BIGELOW, M. (1944) *Proc. Soc. exp. Biol.*, 3, 49.

(c) the metabolism of the tissue, and (d) the arterial blood supply, with its central heating effect. By comparing muscle temperatures at corresponding points, and equal depths from the surface in the two legs, with the patient at rest, the first three factors are eliminated and any temperature differences between the two sides may be taken as an indication of differences in the blood flow.

*Method.*—Two hypodermic needles,  $1\frac{1}{2}$  in. long, were threaded with insulated copper and constantin wires, the ends of which were soldered together so that their junction lay in the bevel of the needle. A third junction was fitted inside a thermos flask containing water at  $37^{\circ}$  C. The wires from the needles and the flask were connected with a Cambridge spot galvanometer through a three-way switch in such a way that either of the needle electrodes could be compared with the constant. The galvanometer had a resistance of 24 ohms, and its sensitivity when damped with an external resistance of 100 ohms was 2 cm. per micro-amp.

The subject's legs were exposed to room temperature. Intradermal injections of procaine were made at corresponding points over the quadriceps, biceps femoris, upper end of tibialis anterior, and gastrocnemius. A thermo-junction needle was inserted to its full depth, one into each leg, at these spots. It was thus possible to compare the temperature of each side with the constant and thus to estimate any difference which might exist in the temperatures of the two limbs by reference to a table obtained by previous calibration of the galvanometer.

The range of temperature differences existing between corresponding points in the two legs was determined in twenty normal persons (Table I), and was found to average

TABLE I.—TEMPERATURE DIFFERENCES IN THE LEGS IN 20 NORMALS. RECORDED IN FRACTIONS OF DEGREES C. AVERAGE DIFFERENCE  $0.08^{\circ}$  C.; MAXIMUM DIFFERENCE  $0.2^{\circ}$  C.

| Case          | .. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 |
|---------------|----|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|----|----|
| Quadriceps    | .. | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  |
| Biceps fem.   | .. | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  |
| Tib. anterior | .. | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  |
| Gastrocnem.   | .. | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  |

TABLE II.—TEMPERATURES OF MUSCLES IN PAINFUL LEG IN TERMS OF THE TEMPERATURE AT EQUIVALENT POINTS IN THE OPPOSITE LIMB, EXPRESSED IN FRACTION OF A DEGREE CENTIGRADE.

| Case | Root | Wasting                 | Temperature differences |             |             |           |
|------|------|-------------------------|-------------------------|-------------|-------------|-----------|
|      |      |                         | Quad.                   | Biceps fem. | Gastrocnem. | Tib. Ant. |
| 1    | L.5  | Nil                     | — 0.2                   | equal       | — 0.1       | + 0.1     |
| 2    | L.5  | Nil                     | — 0.1                   | — 0.2       | + 0.2       | — 0.2     |
| 3    | S.1  | Nil                     | + 0.1                   | — 0.2       | — 0.2       | — 0.1     |
| 4    | S.1  | Calf $\frac{1}{2}$ in.  | equal                   | — 0.3       | — 1.0       | — 0.2     |
| 5    | S.1  | Calf $\frac{1}{2}$ in.  | — 0.1                   | — 0.4       | — 0.8       | — 0.15    |
| 6    | L.5  | Thigh $\frac{1}{2}$ in. | + 0.2                   | — 0.6       | — 0.6       | — 0.1     |
| 7    | L.5  | Calf $\frac{1}{2}$ in.  | + 0.2                   | — 0.2       | — 0.2       | — 0.2     |
| 8    | S.1  | Calf $\frac{1}{2}$ in.  | equal                   | — 0.8       | — 0.4       | + 0.2     |
| 9    | L.5  | Thigh $\frac{1}{2}$ in. | — 0.2                   | — 0.6       | — 1.2       | — 0.1     |
| 10   | S.1  | Calf $\frac{1}{2}$ in.  | + 0.15                  | — 0.4       | — 1.0       | — 0.15    |
| 11   | S.1  | Calf $\frac{1}{2}$ in.  | + 0.2                   | — 0.5       | — 0.7       | + 0.1     |
| 12   | L.5  | Thigh $\frac{1}{2}$ in. | — 0.1                   | — 1.0       | — 0.4       | — 0.4     |
| 13   | L.5  | Calf $\frac{1}{2}$ in.  | — 0.15                  | — 0.3       | — 0.7       | — 0.2     |
| 14   | S.1  | Thigh $\frac{1}{2}$ in. | + 0.2                   | — 0.4       | — 1.0       | — 0.3     |

$0.08^{\circ}$  C., with a maximum deviation of  $0.2^{\circ}$  C. Similar observations were then made in 14 cases of unilateral sciatica, in whom the diagnosis of disc herniation was subsequently confirmed at operation (Table II). In 4 cases there was no significant

Interrupted galvanism has been the therapy of choice in the treatment of peripheral nerve injuries. It is usually necessary to employ the longitudinal reaction, with the electrodes placed in such a way that the best possible muscular contraction is obtained. Unfortunately, daily therapy results in ionic burning, which necessitates either a reversal of the current or an alteration in the position of the electrodes, both alternatives causing a less adequate contraction.

Was there perhaps some method of solving the problem of ionic burning without moving the electrodes or reversing the current? Our technicians were consulted, and produced in 1944 a machine which they called the "balanced pulse generator". It dispensed a square-topped pulse of 300 milliseconds' duration at a repetition rate of 30 per minute. In the intervals between the stimuli, the current was automatically reversed by the machine in order to cancel out any ionization, this reversed current being subliminal and occupying the remainder of the period between stimuli. Diagrammatically this can be represented as follows (see fig. 1): The duration of the

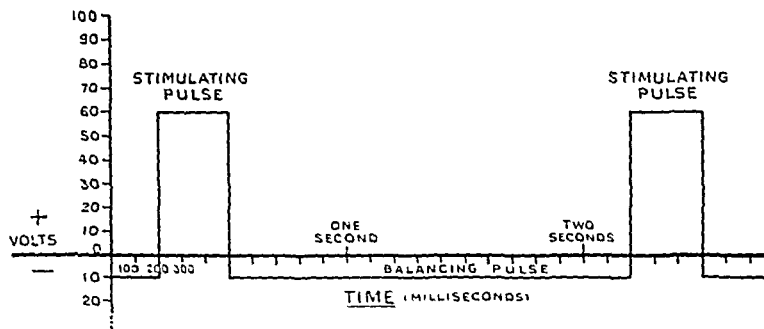


FIG. 1.—Diagrammatic representation of balanced pulse principle.

impulse of 300 milliseconds had been arrived at mainly by trial and error, using pulses in a gradation of 100 milliseconds, from 100 milliseconds to 1 second. The 300 millisecond pulse was considered the one which gave the most adequate contraction and which was also borne most comfortably by the patient. Chemical tests such as the use of litmus paper under the electrodes proved that no ionization occurred, and this was borne out in therapy. We were thus able to stimulate our denervated muscles for periods of ten to twenty minutes twice a day, or even more often if we desired. Treatment by means of the balanced pulse generator rapidly became the method of choice in our physiotherapy departments and rehabilitation centres when interrupted galvanism was called for, and was soon popular among physiotherapists and patients alike.

In January 1947 we met to consider an improved design of balanced pulse generator. Several commercial designs of thermionic valve stimulator were considered. We felt that we could improve our own balanced pulse generator by the addition of pulses of various lengths and frequencies, still utilizing the balanced pulse principle. The feeling of us all was that such a machine would materially increase the scope of electrotherapy. It would also provide a diagnostic set for the plotting of intensity-duration curves. Ritchie [5] and Bauwens [1] had published their results on the use of graduated pulses for diagnostic purposes, but at this time no investigations had been carried out on the therapeutic value of such pulses. We were proposing to combine diagnostic and therapeutic properties in one machine, a scheme which we realized would be open to criticism. The accent, however, was on therapy and not diagnosis, and our ultimate aim was the production of a combined table, using thermionic valve circuits, which we felt would have many advantages over existing

*(May 11, 1949)*

## **Electrodiagnosis and Electrotherapy in the Royal Air Force**

Dr. Basil Kiernander introduced the speakers at the Meeting. He said that in view of the great interest being displayed generally in electromyography and in electronic stimulators, and the variety of such machines being made by manufacturers, a critical evaluation of these would be most useful.

The speakers would show first, the development of the electronic stimulator and secondly, the development of the electromyograph.

Dr. Kiernander pointed out that the R.A.F. Medical Service had not allowed their Physical Medicine organization to disappear or even to deteriorate since the end of the war. In fact, on the contrary, owing to the sympathy of the R.A.F. in general, and particularly of the Director-General of Medical Services, they had been enabled to develop further, under adequate specialized medical direction, Physical Medicine Departments throughout the R.A.F. Quite apart from the clinical practice that was provided, they had been steadily training both Specialists in Physical Medicine from regular R.A.F. medical officers and also physiotherapists. In addition, research was being carried out clinically on quite a large scale and also experimentally in the laboratories at the Technical Repair and Development Section, R.A.F., Chessington.

The D.G.M.S. had been most helpful in the development of the policy of research in Physical Medicine; Mr. Brennand had put an immense amount of work into the production of the sets which would be demonstrated and other apparatus at the Technical Repair and Development Section, Chessington, and his, Dr. Kiernander's, colleague, Mr. Osmond Clarke, Civilian Consultant in Orthopaedics to the R.A.F., had given valuable advice. The two Service Specialists in Physical Medicine, S/Ldr. Mason and F/Lt. Richardson, whose papers they were going to hear, had done an enormous amount of clinical work, investigating and surveying the value of these new instruments, while keeping in full liaison with Sir Morton Smart and Dr. Kiernander, their civilian colleagues in the R.A.F. whose services had been freely available for advice and consultation.

## **Some Aspects of Electrodiagnosis and Electrotherapy in the Royal Air Force**

By Squadron Leader E. F. MASON, M.B.E., M.B., Ch.B., D.Phys.Med.

ORTHOPÆDIC Surgery and Physical Medicine in the Royal Air Force are predominantly concerned with the treatment of trauma among males between the ages of 18 and 40 years. The majority of these men are skilled and therefore valuable tradesmen, whether they be air crew or ground crew. During the war it was necessary for us to attempt to get them back to their jobs as quickly as possible, and among other things, we built up a comprehensive rehabilitation service to cater for this problem.

There were, in the Royal Air Force, many-skilled technicians, to whom we might well apply the term "Back-room boys", who were concerned, among other things, with the intricacies of electrical installations, especially radar, and it is to them we turned in search of improved methods to apply to both electrodiagnosis and electrotherapy. A special medical research unit, now known as the Technical Repair and Development Section, was formed. It is the results of the endeavours of this Section to meet our medical demands which my colleague and I wish to discuss, and I cannot praise too highly their technical advances both during the war, and since.

The trauma suffered by many personnel, especially air crew, caused peripheral nerve damage, a type of injury which results in many months of disability. A special peripheral nerve injury centre was created at one of our main hospitals. The work of Gutmann and Guttmann [2] in 1942 had shown that adequate electrical stimulation of denervated muscles slowed down the process of atrophy of muscle fibres, and this was supported by the work of Bowden and Gutmann [3] in 1944, and by Jackson and Seddon [4] in 1945. They showed that atrophy is most rapid in the early stages of paralysis, and that electrotherapy reduces the rate of connective tissue formation. The general conclusion drawn by these workers was that it is essential that electrotherapy should not only be regular and adequate, but should begin as soon as possible after nerve injury. It was impossible to say whether electrotherapy, adequately applied, would cut down the time of recovery.

both with physiotherapists and patients. It has proved to have two main advantages over existing methods of muscular stimulation. First, a more adequate contraction can be obtained, secondly, there is less patient-discomfort. All physiotherapists agree that the pulses in the faradic band, namely the 3, 1, and 0.3 millisecond pulses, give a far more adequate contraction than the induced current when stimulating groups of small muscles, such as forearm and hand muscles. Some patients state that they feel the impulse is too sharp, has too much of a kick in it, but all prefer it to conventional faradic stimulation. Groups of large muscles, such as quadriceps, can be satisfactorily stimulated also. Here it appears that patient-discomfort is largely dependent on electrode size.

The galvanic pulses have proved extremely valuable for paralysed small muscles, and have the added advantage of eradicating ionic burning. Some patients again state that the stimulus is too sharp.

In several cases of anterior poliomyelitis with commencing muscle recovery, and before contraction to pulses in the faradic band can be obtained, the shorter galvanic pulses have proved the more effective, so that there is apparently an "optimum" pulse, which can be applied to this particular stage of recovery. Sufficient investigation, however, has not yet been carried out to determine whether this is so.

The stimulator has proved entirely satisfactory for the drawing of I.T. curves, although I have not yet investigated a sufficient number of cases to be of statistical value. Ordinary everyday usage in a busy physiotherapy department has not affected the accuracy of the set, and a recent technical test has shown that the pulses are within  $\pm 5\%$  of the accuracy obtained when the set was constructed. [The set was shown to the meeting.]

Our next development was to split off from the parent set, the separate faradic and galvanic functions, and especially was this so with the faradic component which had proved so excellent in practice. The faradic stimulator is a small, easily portable machine which generates a square wave form of one millisecond's duration. The pulse is interrupted 50 times a second and surged electronically 30 times a minute.

Cathode-ray oscilloscope displays show the differences between the damped oscillation of the induced current and the square-wave form of the stimulator (figs. 3 and 4). The design is such that alteration of pulse recurrence and surging rates



FIG. 3.—Unmodulated output of conventional faradic coil (Surge off). The amplitude and duration of the wave train depend on the patient's resistance.

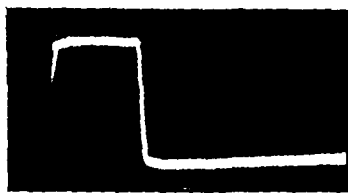


FIG. 4.—Unmodulated output of the Type 3 electronic stimulator. Note that the edge duration is small, thus enabling stimulus time to be specified regardless of pulse amplitude.

can be easily made, if required by some future technique. The set has been subjected to severe clinical tests in two busy physiotherapy departments, and since July 1948, in my department alone, 1,327 faradic trials have been made. In my opinion it is superior to faradic stimulation as obtained from the more conventional types of apparatus. I have not found a single patient who does not prefer it to the induced current generator. All physiotherapists have been impressed with the excellence of the automatic surging device, since the only manipulation required is control of the large, voltage-calibrated dial. Using the cathode-ray oscilloscope in parallel with the

models, and would also provide the means for testing for the new reaction of degeneration, namely, by the drawing of intensity-duration curves. The set (see fig. 2) became available for preliminary clinical trials in June 1947, and on August 15 I received it at the R.A.F. Rehabilitation Centre at Mongewell Park. The set provides:

- (1) A range of pulses 0.03, 0.1, 0.3, 1, 3, 10, 100, 300 milliseconds.
- (2) Surging of the 100 and 300 millisecond pulses at 30 per minute.
- (3) Interruption of the short pulses (0.03, 0.1, 0.3, 1) at 50 per second with surging at 30 per minute.
- (4) Continuous galvanic output for ionization therapy.
- (5) For diagnostic purposes, pulses of established accuracy which can be applied without surging.

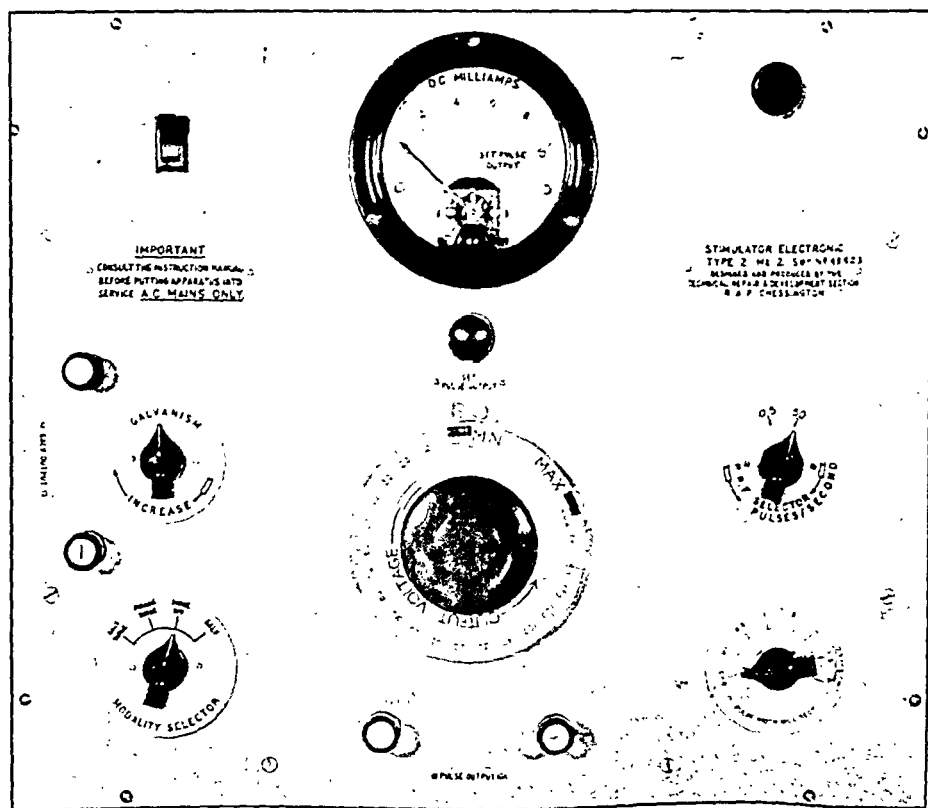


FIG. 2.—The combined diagnostic and therapeutic stimulator.

All pulses are balanced, thus eliminating skin reaction.

Output calibration is practically unaffected by mains supply changes, valve deterioration, or patient-resistance or -capacity. The output is high—200 volts peak to peak—controlled by a large directly calibrated dial. In therapeutic use, any particular pulse can be selected quickly and easily, since voltage and pulse duration are accurately known. An electronic surging circuit is incorporated, which is superior to contemporary mechanical surgers in that an adequately long rest period between consecutive surges is provided, and there are no moving parts or contacts to wear or cause radio interference. The equipment is completely silent in operation. The set has been used mainly in cases of recovery from peripheral nerve injury and cases of anterior poliomyelitis, and since I began to use it, has become extremely popular

## Clinical Electromyography in the Royal Air Force

By Flight Lieutenant A. T. RICHARDSON, M.B., B.S.

THE particular aspect of electrodiagnosis in the Royal Air Force that I wish to present is clinical electromyography. The pioneer work of Piper in 1912 [1] set the subject going in Germany. In this country the work of Adrian presented in his Oliver Sharpey Lectures of 1925 [2] and later his work with Bronk [3] did much to define the physiological basis upon which myography rests. To record muscle action potentials these early workers used string galvanometers, detecting the muscle potentials at first by surface electrodes and later, after their introduction by Rehn in 1921, by needle electrodes.

It is, however, more recently that developments in electronic apparatus have made possible electromyographic units suitable for clinical work. Two units are notable in this respect, viz.:

(1) The single channel unit with loud-speaker and cathode-ray tube which is outstandingly easy to operate and free from extraneous interference, used by Weddell, Feinstein and Pattle at Oxford [4].

(2) The double channel unit with needle and surface electrodes providing accurate calibration, recording and stimulation, demonstrated by Bauwens last year to the Section of Neurology of this Society [5].

The evolution of electromyography from the physiological laboratory to the consulting-room seemed to offer to us, in the Physical Medicine Section of the Royal Air Force, a new approach to our Service problems. The investigation of peripheral nerve injuries, lower motor neurone disease and the assessment of physical disability resulting from such lesions are among our most difficult problems. Therefore, in June 1945, a portable myophone was constructed, consisting of a concentric needle electrode, amplifier and speaker. It had two serious limitations: the lack of accurate calibration with which to measure the duration and amplitude of muscle potentials and, above all, the high-pitched tone of the speaker, which made the differentiation of potentials by sound difficult. More recently a single channel myograph kindly lent to us by Dr. Bauwens was in routine use until replaced by that shown in fig. 1. This apparatus produced by the Technical Repair and Development Section of the Royal Air Force Medical Branch was designed primarily for clinical work. Most of the variable controls are pre-set, requiring only periodic adjustment by a technician, and so no great technical knowledge is needed to use the apparatus. We do not find, however, the same ease in relating the potentials to pathological conditions. The apparatus has twin channels, each channel having a concentric needle electrode and a pair of surface electrodes which are retained in position by suction. The potentials detected by the electrodes of each channel are amplified, relayed through a meter, which measures the peak to peak voltage, and are finally fed to a loud-speaker and to one beam of the cathode-ray tube display. The other channel, of course, feeds the other beam of the cathode-ray tube. This cathode-ray tube is a 12 in. short persistence, single beam type, but it is equipped with an electronic beam switch, so that phenomena occurring on both channels may be viewed simultaneously. In addition the potentials from one channel are recorded on magnetic tape.

There is one main selector switch which controls the functions of the entire unit; this switch may be moved into five positions:

In the first position, a 500 cycle per second calibration sine wave of variable known amplitudes is projected in the place of the input from the muscle electrodes to the amplifier. Because this calibration wave goes through the same amplifier as the input from the electrodes, it is exactly comparable with the input at any amplification,

patient, we obtained the following results from the surging of a conventional set and from the stimulator (see figs. 5 and 6). In my opinion there is no doubt that this type of stimulator will eventually replace the faradic machines at present in use.

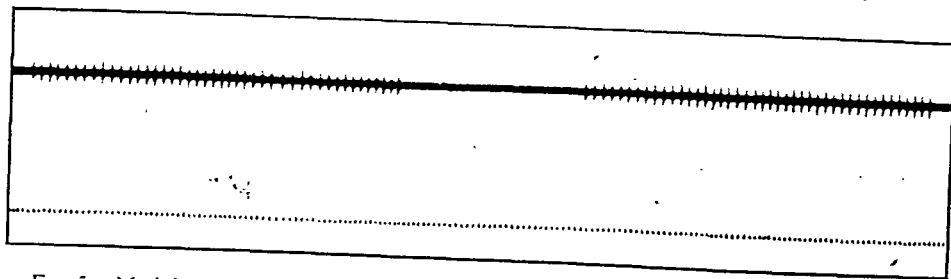


FIG. 5.—Modulated output of conventional coil (Surge On). Note that the ratio between maximum and minimum amplitudes during the "On" period is low. This ratio will vary inversely as the patient-resistance. (In the above test 5,000 ohms.)

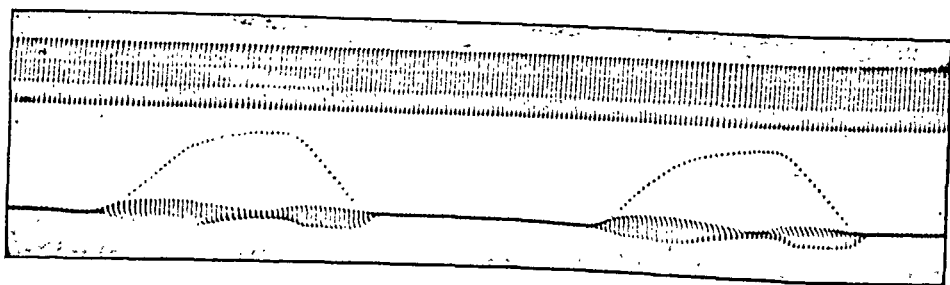


FIG. 6.—Modulated pulse output of the Type 3 stimulator. Note the long rest period between consecutive surges.

FIGS. 3, 4, 5 and 6 are untouched photographs of cathode-ray tube displays. Figs. 3 and 4 were taken with a high speed synchroscope. In figs. 5 and 6 the second beam displays a 50 cycle sine wave time mark.

We are still in the process of developing the new galvanic stimulator which will be an improved version of the old balanced pulse generator.

It is not suggested that these devices represent the last word in electrical stimulation of nerve and muscle. There is as yet no proof that the square-wave form is the best shape of impulse and, in fact, it would appear that a less steeply rising wave front may give an equally adequate muscular contraction, whilst adding even further to the comfort factor for the patient. Not until we can accurately generate an impulse which will produce in tissues a stimulus similar to that generated by our own nervous systems, can we hope to reach the acme of muscular contraction by artificial means.

I wish to acknowledge the encouragement I have received in developing these sets from Mr. H. Osmond Clarke and Group Captain C. J. S. O'Malley, and I wish to thank the Director-General of Medical Services of the Royal Air Force for permission to publish this paper.

#### REFERENCES

- 1 BAUVENS, P. (1941) *Proc. R. Soc. Med.*, 34, 459 and 715.
- 2 GUTMANN, E., and GUTTMANN, L. (1942) *Lancet* (i), 169.
- 3 BOWDEN, R. E. M., and GUTMANN, E. (1944) *Brain*, 67, 273.
- 4 JACKSON, E. C. S., and SEDDON, H. J. (1945) *Brit. Med. J.* (ii), 485.
- 5 RITCHIE, A. E. (1948) *Brit. J. Phys. Med.*, 11, 101.



one that allows an input of 100 microvolts to give a vertical screen deflection of 1 centimetre. In the case of needle electrodes the most useful gain is one that allows an input of 30 microvolts to give a similar screen deflection.

The most convenient calibration wave amplitude is 100 microvolts, this being the dividing line between normal motor unit action potentials and fibrillation potentials. Similarly the calibration wavelength of 2 milliseconds differentiates between the duration of fibrillation and the longer motor unit potentials.

The magnetic tape recorder will record for thirty minutes at a tape-running speed of 8 inches per second, which speed allows accurate recording. It is our practice to keep it running during the entire examination of the patient, this arrangement allowing fleeting muscle potentials, often obtained on moving the needle electrode, to be recorded and analysed at leisure. The tape may be used repeatedly by erasing previous records.

[At the conclusion of the paper the speaker played a recording of potentials they had encountered and the recognition of which had been of value in diagnosis.]

In examining a patient it is our routine first to plot intensity duration curves of the affected muscles. This is done by using a constant voltage type stimulator, which is incorporated in the myograph unit. The reasons for this routine are:

(1) In general the progress of our peripheral nerve injury cases is followed by comparing serial intensity duration curves. I think it will be generally agreed that muscle stimulators are more suited to routine use in peripheral nerve injuries than myographs which are expensive and less easy to use.

(2) In long-standing cases the presence of contractile tissue is assured before needing for fibrillation potentials is undertaken.

(3) Rarely—as in cases of slowly progressive lower motor neurone destruction—cases occur in which fibrillation is difficult to detect, although the intensity duration curve is of the double type indicating partial denervation of the affected muscle.

(4) The stimulator is used to stimulate nerve trunks and thereby to relate the muscle to their nerve supply. This is of the utmost importance in examining the small muscles of the hand.

Following the use of the stimulator the suspected muscles are compared with the corresponding ones of the opposite limb by using surface electrodes. By this means:

(1) Spontaneous potentials in the resting muscles may be detected. Only the larger spontaneous potentials can be detected by surface electrodes, for instance, the fasciculation potentials of motor neurone disease and the potentials in nerve irritation.

(2) The relative strengths of corresponding muscles on maximal voluntary contraction may be determined by comparing the loud-speaker noise, degree of interference pattern on the cathode-ray tube, or meter readings.

(3) An exact measurement of tendon-jerk response may be obtained.

(4) Measurements of nerve conduction time and the strength of muscle contraction on nerve trunk stimulation may be obtained, the contraction in this instance being a synchronous contraction of the motor units of the muscle. To allow us to follow the recovery of nerve lesions by measuring the strength of muscle contraction on stimulation of the nerve trunk week by week, we place the surface electrodes in standard positions. Variations occur, however, partly due to the fact that regenerating nerves have a slower conduction time and because of this, the contraction of their motor units occurs after the contraction of normally innervated motor units and

either by reference to the meters, or to the cathode-ray tube. In the second position of the main selector switch, the calibration wave is projected similarly along the second channel. In the third position of the main control, the amplifiers connect with the muscle electrodes. This is the position used when detecting muscle potentials, and thus, by moving the main selector switch, the known calibration wave and the input from the muscle electrodes may be interchanged at will and the comparison made, from which the amplitude and duration of the muscle potentials may be determined. In the fourth and fifth positions of the selector switch a balanced pulse stimulus can be supplied along either needle electrode. This stimulus has a square

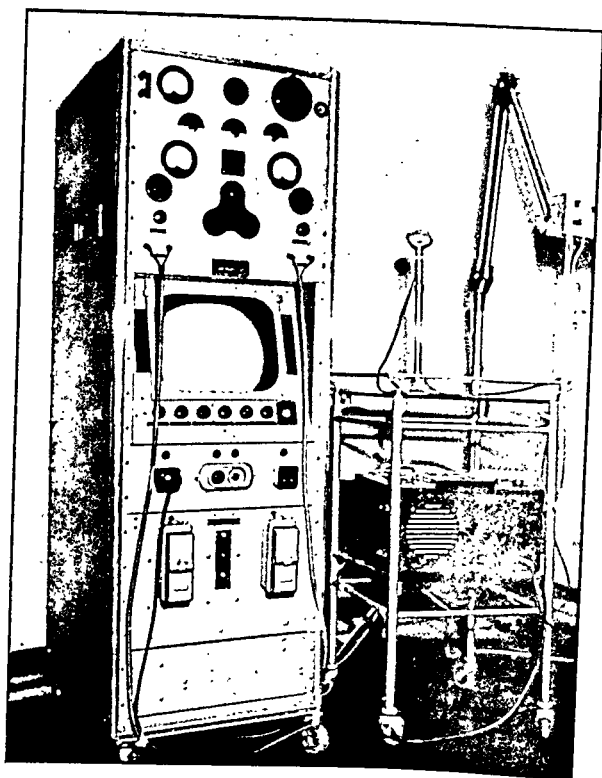


FIG. 1.—The electromyograph in use in the Royal Air Force.

pulse form of 100, 30 or 10 milliseconds' duration and variable amplitude between zero and 200 volts, its repetition rate being 30 per minute. The use of this stimulus to produce contraction of the muscle in which the needle is embedded allows the operator to identify the muscle which is being tested; a matter of some difficulty in the forearm and hand.

Each channel has 7 amplifier valves arranged so as to afford a high degree of rejection of unwanted signals, in fact, a rejection ratio of approximately 26,000 to 1 exists. The amplifier response is linear from 20 to 10,000 cycles per second and the noise level is normally less than 5 microvolts peak to peak with patient connected. The gain controls, one for each amplifier, are calibrated directly in microvolts per centimetre vertical screen deflection of the beams of the cathode-ray tube and give gains varying in six steps from zero to 10 microvolts per centimetre deflection. In our experience the amplification gain most useful when using surface electrodes is

one that allows an input of 100 microvolts to give a vertical screen deflection of 1 centimetre. In the case of needle electrodes the most useful gain is one that allows an input of 30 microvolts to give a similar screen deflection.

The most convenient calibration wave amplitude is 100 microvolts, this being the dividing line between normal motor unit action potentials and fibrillation potentials. Similarly the calibration wavelength of 2 milliseconds differentiates between the duration of fibrillation and the longer motor unit potentials.

The magnetic tape recorder will record for thirty minutes at a tape-running speed of 8 inches per second, which speed allows accurate recording. It is our practice to keep it running during the entire examination of the patient, this arrangement allowing fleeting muscle potentials, often obtained on moving the needle electrode, to be recorded and analysed at leisure. The tape may be used repeatedly by erasing previous records.

[At the conclusion of the paper the speaker played a recording of potentials they had encountered and the recognition of which had been of value in diagnosis.]

In examining a patient it is our routine first to plot intensity duration curves of the affected muscles. This is done by using a constant voltage type stimulator, which is incorporated in the myograph unit. The reasons for this routine are:

(1) In general the progress of our peripheral nerve injury cases is followed by comparing serial intensity duration curves. I think it will be generally agreed that muscle stimulators are more suited to routine use in peripheral nerve injuries than myographs which are expensive and less easy to use.

(2) In long-standing cases the presence of contractile tissue is assured before needling for fibrillation potentials is undertaken.

(3) Rarely—as in cases of slowly progressive lower motor neurone destruction—cases occur in which fibrillation is difficult to detect, although the intensity duration curve is of the double type indicating partial denervation of the affected muscle.

(4) The stimulator is used to stimulate nerve trunks and thereby to relate the muscle to their nerve supply. This is of the utmost importance in examining the small muscles of the hand.

Following the use of the stimulator the suspected muscles are compared with the corresponding ones of the opposite limb by using surface electrodes. By this means:

(1) Spontaneous potentials in the resting muscles may be detected. Only the larger spontaneous potentials can be detected by surface electrodes, for instance, the fasciculation potentials of motor neurone disease and the potentials in nerve irritation.

(2) The relative strengths of corresponding muscles on maximal voluntary contraction may be determined by comparing the loud-speaker noise, degree of interference pattern on the cathode-ray tube, or meter readings.

(3) An exact measurement of tendon-jerk response may be obtained.

(4) Measurements of nerve conduction time and the strength of muscle contraction on nerve trunk stimulation may be obtained, the contraction in this instance being a synchronous contraction of the motor units of the muscle. To allow us to follow the recovery of nerve lesions by measuring the strength of muscle contraction on stimulation of the nerve trunk week by week, we place the surface electrodes in standard positions. Variations occur, however, partly due to the fact that regenerating nerves have a slower conduction time and because of this, the contraction of their motor units occurs after the contraction of normally innervated motor units and

escape measurement by the meters. The detection of spontaneous potentials in muscles in cases of nerve root irritation, for instance, by cervical and lumbar prolapsed intervertebral discs and osteoarthritis of the spine, is in our experience, inconstant. In cases in which they do occur, there is often a latent period of five to ten minutes after movement of the spine into the position of maximal symptoms before the "chugging" potentials occur. Although, in the cervical region particularly, an accurate localization of the root being irritated may be obtained, the use of myography in this way seems limited. We have found of more diagnostic value in motor nerve root pressure, the reduction of motor unit activity on maximal voluntary contraction, as a general rule, unaccompanied by fibrillation. In the cases of muscle atrophy due to cord lesions we have examined, fibrillation has always been found, although sometimes with difficulty.

The use of needle electrodes, and by that means the recognition of potential types and their relative preponderance, seems to us to offer the most valuable method of myographic diagnosis. In using needles, we have not found a local anæsthetic necessary, as the patients tolerate the fine needle electrodes well. In nervous patients a short-acting barbiturate as a sedative and aspirin are all that is required, at any rate in the average member of the Royal Air Force and Women's Royal Air Force.

As the scope of this paper is clinical myography, I would like to mention the potential types which can be easily recognized, and the significance of which is now generally agreed.

(1) *Normal motor unit action potentials.*—These are obtained:

(i) By insertion of the needle electrode into a motor unit with a nerve supply which has not degenerated. These are referred to by Weddell as motor unit insertion potentials.

(ii) On voluntary contraction of the muscle, the occurrence of repetitive normal motor unit potentials at a gradually increasing frequency with developing tension is quite characteristic. The detection of these potentials in lower motor neurone lesions, indicating that some neurones are in continuity, is of prime importance, denoting as it does an incomplete lesion. The lack of motor unit potentials on insertion or volition does not necessarily mean that nerve continuity is broken, because the sheath may still be intact, although the neurones have undergone degeneration; hence exploration may show a nerve in continuity although the myograph suggests otherwise. The reduction of motor unit activity represented by lack of the normal interference pattern across the screen on maximal contraction allows assessment of the degree of damage. The normal interference pattern is produced by out of phase activity of many motor units and loss of this indicates a neuropathic or myelopathic atrophy.

Fasciculation potentials and other spontaneous potentials detected by surface electrodes may be localized accurately by the use of needle electrodes.

(2) *Fibrillation potentials.*—These small potentials, producing rhythmic clicking sounds in the loud-speaker, are easily recognized and occur on insertion of the needle or spontaneously. Their presence, indicating lower motor neurone degeneration with contractile tissue still present, is remarkably constant if the muscles are first warmed to blood temperature, although occasionally we have not detected them until we have used prostigmine. Our experience has shown that the detection of these potentials is a most sensitive index of denervation and they are often detected in muscles which are normal to all other tests, including the plotting of the intensity duration curves. The following case-history illustrates this:

A F/Lt., aged 37, was taken ill while serving in Iraq. He gave a history of diarrhoea and vomiting and three days later he noticed a tendency for the (R) foot to drop. He was invalided home, by which time although he complained of weakness in the (R) dorsiflexors, this was not convincing on clinical examination. The intensity duration curve was completely normal. Fibrillation potentials were, however, detected, indicating the organic basis for his complaints. It will be a matter of interest that synchronization of motor unit potentials was obtained in this case, although atrophy of the muscle could not be demonstrated clinically.

The value of detecting fibrillation potentials to localize the lesion is obvious; we have found this of particular value in non-traumatic peripheral nerve lesions, such as those following serum injections.

(3) *Complex potentials.*—We have seen complex potentials in three circumstances:

(i) Normal polyphasic motor unit potentials.

(ii) Fibrillation or motor unit potentials occurring near together and giving the appearance of complex potentials, the former occurring spontaneously and the latter on contraction. Generally, however, it is only a brief time before the units go out of phase.

(iii) Complex potentials found during recovery and sometimes during degeneration. There is also the complex wave form occurring on stimulation of the nerve trunk in recovering nerve lesions. We have found it of great value to detect these potentials which are one of the earliest signs of re-innervation. They continue to be found for a considerable time after functional recovery, particularly has this been noticeable after acute anterior poliomyelitis. The complicated pattern of many complex potentials in a lesion recovering well contrasts with the sparse complex potentials of a poorly recovering lesion. These complex potentials appear on attempted voluntary contraction and in recovery they are soon followed by the appearance of easily fatiguing motor units. We have also found the decrease in the number of fibrillation potentials which precedes recovery, and which is followed by complex potentials, a most valuable sign.

In conclusion, I would like to make a passing reference to several phenomena, the significance of which is not generally agreed.

(1) Trains of high-frequency potentials which sound like a diving aeroplane. These potentials are often small, of dimensions comparable with fibrillation potentials, and would seem, therefore, to be due largely to the contraction of individual fibres. We have obtained them on mechanical irritation of the muscle by needle electrodes in cases of progressive muscular atrophy and dystrophia myotonica and in one instance in a case of anterior poliomyelitis.

(2) Double potentials. We have encountered these in peripheral nerve injuries, poliomyelitis and motor neurone disease. The pathological significance seems doubtful.

(3) Synchronization of motor unit activity. The recognition of synchronization was first applied to clinical work by Buchthal and Clemmesen [6] who suggested that its cause was the spread of impulses from one neurone to an adjoining neurone in the cord. More recently, Denny-Brown [7] has suggested that the phenomenon of synchronization is not due to synchronous contraction of two or more motor units, but to the detection by two or more needle electrodes of the same large unit. This, he says, is made possible by the loss of the smaller units whose discharge normally smoothes the action of the larger unit; to the coarse tremor produced by these large units on contraction he gave the name "Contraction Fasciculation". Whatever the explanation may be of synchronization there can be no doubt about the ease with which it is detected in anterior poliomyelitis and the extreme difficulty with which it is detected, if at all, in the normal person or in peripheral nerve injuries. Since using a

double channel myograph, we have examined 11 cases of acute anterior poliomyelitis and found synchronization in all of them. However, we have not found it possible in this small series of cases, to prove that more than one, often large, unit was contracting. We attempted this proof by applying the localizing properties of the needle electrode, searching for independent rhythm of one of the units and attempting to make one of the units drop out by fatigue.

We are therefore of the opinion, that in the present state of our knowledge electromyography is of proved value in peripheral nerve injuries and disease, in that it can provide concrete evidence of nerve damage recovery and retention of any function before these phenomena can be estimated clinically.

I wish to acknowledge the help that we have received from Dr. Bauwens and his technical assistant, Mr. Peter Styles, of St. Thomas's Hospital, in bringing myography into use in the Royal Air Force. I wish to thank the Director-General of Medical Services of the Royal Air Force for permission to read this paper.

A demonstration of recordings showing normal motor unit potentials, fibrillation potentials and the complex potentials associated with recovery was given.

Some examples of fasciculation potentials obtained from a case of progressive muscular atrophy and some recordings from a case of dystrophia myotonica were also included.

#### REFERENCES

- 1 PIPER, H. (1912) *Elektrophysiologie menschlicher Muskeln*. Berlin.
- 2 ADRIAN, E. D. (1925) *Lancet* (i), 1229, 1282.
- 3 ———, and BRONK, D. W. (1929) *J. Physiol.*, 67, 119.
- 4 WEDDELL, G., FEINSTEIN, B., and PATTLE, R. E. (1944) *Brain*, 67, 178.
- 5 BAUWENS, P. (1948) *Proc. R. Soc. Med.*, 41, 291.
- 6 BUCHTHAL, F., and CLEMMESEN, S. (1943) *Acta psychiat., Kbh.*, 18, 377.
- 7 DENNY-BROWN, D. (1949) *Arch. Neurol. Psychiat., Chicago*, 61, 99.

## Section of Orthopædics

President—H. J. SEDDON, M.A., D.M., F.R.C.S.

[March 1, 1949]

**Arthritis of Wrist Relieved by Synovectomy.**—M. C. WILKINSON, M.B.

Mrs. A. D., aged 26.

About September 1947 pain and swelling of right wrist, and during December 1947 of proximal interphalangeal joint of right index finger also. Recommended for admission in February 1948 but not admitted until October 1948; during this time condition got worse and she became incapacitated for work; plaster wrist splint provided in July 1948 alleviated the pain.

*Condition on admission.*—Considerable puffy swelling around wrist, all movements of wrist restricted and painful. Swelling of proximal interphalangeal joint of right



FIG. 1.

index finger: flexion to 90 degrees. W.R. negative. GCFT negative. Mantoux positive. X-ray lungs normal. X-ray of right wrist shown in fig. 1. All joint spaces of the carpus and wrist are narrowed, and the arthritis is probably rheumatoid. In tuberculosis, the carpo-metacarpal joints are usually affected first.

18.10.48: Operation. As much synovial membrane as possible was removed through a dorsal incision; found to be very thick and œdematous. No caseation or tubercles seen.

*Microscopical report.*—Heavy plasma-cell and lymphocytic infiltration in portion of synovial membrane.

6.11.48: Three weeks after operation—wrist felt much better. Finger improved. No post-operative splintage except bandage; movements encouraged.

21.11.48: Discharged six weeks after admission, with wrist splint to wear in case of pain.

January 1949: Splint discarded. Work resumed. Movements of wrist increased; no synovitis; no pain; condition of interphalangeal joint unchanged.

### **Osteotomy of the Spine in the Treatment of Severe Dorsal Kyphosis: Four Cases.—**

W. ALEXANDER LAW, O.B.E., M.D., F.R.C.S.

The spinal osteotomy operation was devised by M. N. Smith-Petersen (1945, *J. Bone Jt. Surg.*, 27, 1) to enable patients with rigid kyphosis to resume the erect position, or resume a position sufficiently erect to see ahead. Although the kyphosis in cases of ankylosing spondylitis is greatest in the dorsal region, there are also rigidity and flattening with loss of lordosis in the lumbar region, which accentuate the deformity.

The operation is carried out in the lumbar region, at one or more levels, in one or more stages. The whole operation is performed by the dorsal route, there being no second stage with an anterior approach necessary. The lumbar region is chosen for this operation on account of the greater width of the spinal canal and the smaller contents of the spinal canal below the lumbar enlargement of the cord. In addition, in the dorsal region the fused costovertebral joints handicap correction, although in cases of dorsal kyphosis resulting from Scheuermann's disease the osteotomy carried out in this region is a perfectly sound and feasible procedure.

The operation is performed in the lumbar region therefore, at levels showing a minimum of bony wedging, the excess bone formed in the interlaminar ligaments being excised together with wedges from the intra-articular facets. After the bone has been resected from the ligamenta flava and remnants of the ligamenta flava detached, a periosteal elevator is passed anteriorly to the lamina and articular process, into the lateral intervertebral notch on each side. The osteotomy is performed through the superior articular process of the vertebra below and the inferior articular process of the vertebra above, in an oblique plane of 45 degrees with the frontal plane. The number of levels is determined by the extent of new bone formation in relation to the facets and intervertebral discs and to the general condition of the patient during the operation. After the osteotomy has been completed, correction is obtained by hyperextending the spine so that the edge of the lamina above slides on to a shelf of the lamina below, without compressing the cord or over-stretching the soft tissues. Spinal fusion is then carried out by raising bone flaps from the adjacent laminae, and utilizing the previously resected bone in the form of cancellous bone chips.

Dramatic results can be achieved by this operation, but great care is essential, particularly in the degree of hyperextension, so as to achieve stability and to avoid extensive stretching of the nerve roots, femoral nerves or vessels. Undue stretching of the autonomic nerves may also result in distension and retention in the early post-operative phase, as may also occur when hyperextension plaster jackets are applied in certain spinal compression fractures.

Following the operation, the patient is immobilized in a plaster jacket, and nursing may be made easier if the thighs are also included. This gives greater stability,



particularly when turning the patient. With the patient in the prone position the greatest care must be exercised to avoid impairment of the respiration or even frank suffocation from bedclothes or pillows, as in many of these cases the patient also has a rigid cervical spine. At an early stage in this series of 9 cases, one patient, after a perfectly successful operation, unfortunately succumbed in this manner.

Later follow-up shows that fusion is readily achieved, as would be expected in cases of ankylosing spondylitis, and that the correction is maintained. Secondary benefits include increase in the vital capacity and alleviation of gastro-intestinal symptoms.

Certain orthopaedic surgeons on the Continent have carried out spinal osteotomy, using both posterior and anterior approaches. Their operation therefore consists of two distinct phases. Using the Smith-Petersen technique a perfectly satisfactory correction can easily be obtained in one stage, the longitudinal ligament rupturing with an audible snap, particularly when it is ossified, and if the osteotomy lines have been made correctly, a perfectly stable relationship is achieved.

#### ILLUSTRATIVE CASES

A film was shown demonstrating the various stages of the operation, particularly the movement at the operation site, when carrying out hyperextension by breaking the operation table.

I.—Thomas D., aged 37. No occupation.

*History.*—Onset of ankylosing spondylitis in 1934, with severe disability for nine years, as a result of which he had to give up his employment as railway boiler washer.

*On examination.*—Bilateral hip flexion deformity of 40 degrees. Arm abduction limited to 90 degrees on right and 70 degrees on left. Spine completely rigid except for a few degrees of rotation of occiput and a few degrees of forward rocking. There was a deformity of over 100 degrees. Chest expansion  $\frac{1}{2}$  in. Movements of temporomandibular joints restricted.

Given course of X-ray therapy during March 1948.

30.8.48: Spinal osteotomy at 3-4 lumbar level. 45 degrees correction obtained.

The initial plaster jacket was causing discomfort so nine days after operation a new one was applied, incorporating the thighs on both sides to give greater fixation; in the course of applying this jacket the degree of correction was extended to nearly 90 degrees. This was accompanied below the knee on left side by a little impairment of sensation but no involvement of quadriceps or hamstring muscle groups.

Patient is now ambulant, free from pain, and is continuing treatment for lower extremities in Department of Physical Medicine.

X-ray of osteotomy site shows increase in bone density, indicative of progressive fusion.

II.—E. M., male, aged 39.

*History.*—Onset of back pain in 1939, with progressive stooping deformity. Treated by deep X-ray therapy and 5 separate doses of thorium X (50 electrostatic units). Complete bony ankylosis of cervical, dorsal and lumbar spine, with fusion of sacro-iliac joints.

5.1.48: Spinal osteotomy at 4-5 lumbar level, using Smith-Petersen technique. A good correction of 45 degrees obtained.

Post-operative recovery complicated by basal collapse of left lung and temporary weakness, with bilateral foot drop, which was postural in origin. Subsequent progress uneventful. Fitted with long spinal brace in June 1948, by which time bony fusion was sound.

Now free from pain and has been fit to resume work during the last eight months, but on account of being in hospital he has lost his job of shop assistant.

III.—B. E., male, aged 51. Civil servant.

*History.*—Onset of stiffness in neck in 1937, subsequently spreading downwards. Treated initially by manipulations. More rapid deterioration in 1946; complete inability to see his way about by June 1947. General symptoms include dyspnoea and flatulence, and he is easily fatigued.

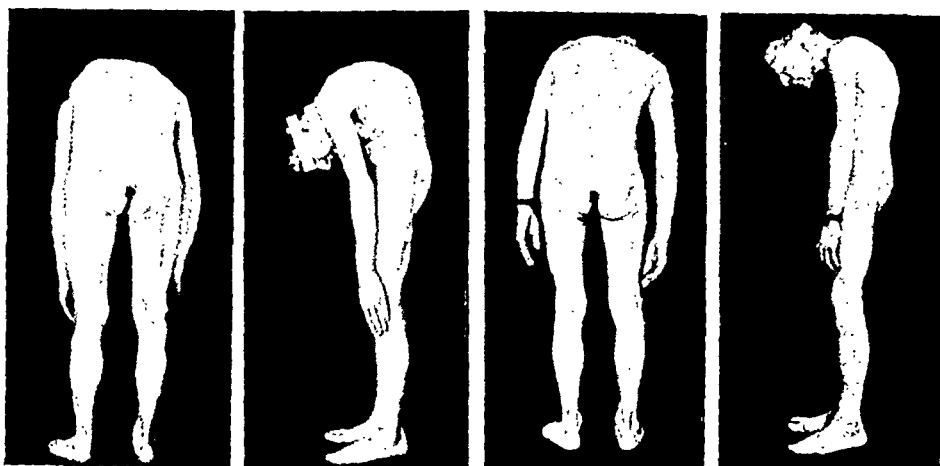


FIG. 1.

FIG. 2.

FIG. 5.

FIG. 6.

*Case III.*—B. E. Pre-operative back and side views (figs. 1 and 2). Post-operative back and side views (figs. 5 and 6). With such a severe deformity as this, further correction may be desirable, at a second operation.



FIG. 3.



FIG. 4.

*Case III.*—B. E. X-rays showing lateral views of dorsal and lumbar spine, with correction at the two levels indicated by the arrows.

*On examination.*—Extreme rigid kyphosis with list to right. Marked abdominal furrow with distension below site of subcostal constriction (figs. 1 and 2). Hip and knee-joint movement reasonably good. Some limitation of shoulder-joint movement.

X-ray shows "bamboo spine" in cervical, dorsal and lumbar regions. Wedging of D.10 and tendency for D.9 to slide forward on D.10 and D.10 on D.11 (fig. 3).

8.11.48: Osteotomy of spine at 2-3 3-4 lumbar levels (fig. 4).

Post-operative recovery uneventful. 45 degrees correction obtained with restoration of lumbar lordosis (figs. 5 and 6).

IV.—H. A. C., male, aged 30. Engineer.

*History.*—Onset of ankylosing spondylitis in 1935 with progressive stoop since 1943. Patient only able to see ahead by bending at knees. Pain in back, breathlessness and indigestion.

Previous treatment included vaccine therapy, 55 treatments of wide-field X-ray therapy between August 1943 and December 1947; 12 doses of thorium X and 8 doses of gold sulphide.

When patient was standing erect the upper part of dorsal spine was almost horizontal. A little movement had been retained in upper cervical spine; complete rigidity in dorsal and lumbar spine. Chest expansion  $\frac{1}{2}$  in. Movement in hip and knee joints retained.

10.1.49: Osteotomy of spine at 3-4 lumbar level. Correction of about 30 degrees obtained.

Post-operative recovery uneventful. Now ambulant in plaster jacket.

#### **Comminuted Fracture-Dislocation of the Shoulder: Result Seven Years After Excision of Fragments and Treatment on Abduction Splint.—L. S. MICHAELIS, M.D.**

In an earlier paper (1944, *J. Bone Jt. Surg.*, 26, 363) I reported on two patients with comminuted fracture-dislocation of the shoulder, who, after excision of fragments, suture of muscle-stumps and after-treatment on an abduction splint, showed very little disability.

Since then the older man has died of intercurrent disease aged 74.

This is a report on the other patient, now aged 64, who returned to work as a gardener two months after operation and who, for the last few years, has earned up to £7 a week as a plasterer's labourer.

He has had no pain or disability although his work involves heavy lifting. Range and power of movement in the shoulder is full although partly achieved in an unorthodox manner. On abduction of the arm the upper end of the humerus undergoes painless subcoracoid dislocation. With the arm hanging free it stands, a new head functionally, opposite the glenoid cavity.

Rotation is well controlled, in fact there is no flailness; the result might be called an arthroplasty of a non-weight-bearing joint with minimum instability.

There is little doubt that no other form of treatment could have proved equally satisfactory.

*Comment.*—Once more it should be emphasized that simple and comminuted fracture-dislocations of the shoulder demand different treatment. In simple cases attempts at reduction or, if these fail, open reduction or arthrodesis are justified although it may be doubted whether the result, both as to painlessness and usefulness, would warrant them. In comminuted cases—the full degree of comminution is not

easily recognized on X-ray films—closed reduction is dangerous to vessels and nerves and senseless because of the certainty of avascular necrosis. Arthrodesis, with the upper 2 in. of the humerus shattered, is impossible. It has to be remembered that comminuted fracture-dislocation differs entirely in its mechanism from the simple form. It is due to direct impact (fig. 1) followed by disruption (fig. 2).

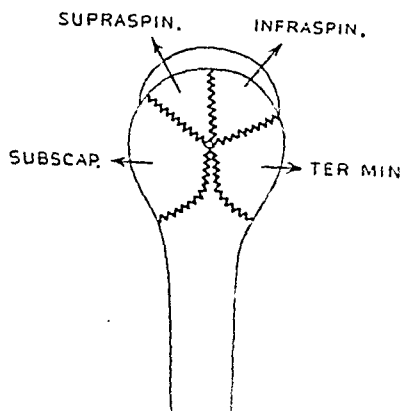


FIG. 1.—Comminuted fracture-dislocation. Lateral view: Stellate fracture main tubercle. Disruption by muscle-pull.

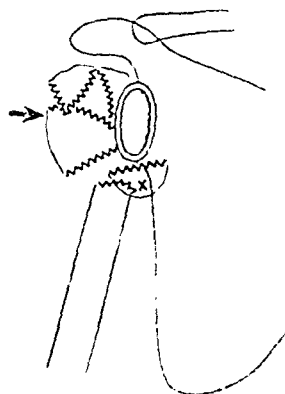


FIG. 2.—A-P. view. → Point of impact. X Avascular head-fragment, loose in "crater".

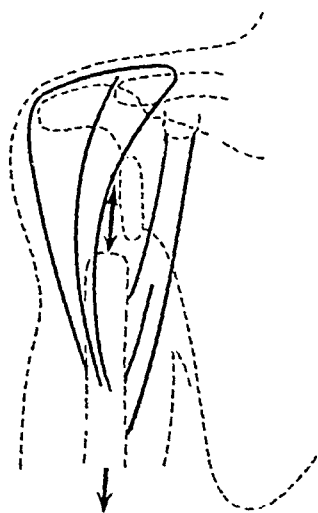


FIG. 3.—Fragments excised. Drag on deltoid, &c., long gap.

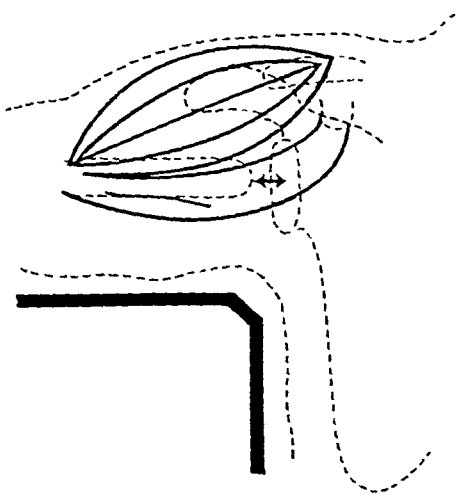


FIG. 4.—On abduction-splint. No drag, short gap.

Excision of fragments is easy to perform. If flailness is to be avoided, the drag of the weight of the arm has to be relieved by an abduction splint for several weeks (figs. 3 and 4). A concentric short scar will form, supported by strong muscles which should be trained for work at a shortened range by early faradism and active contractions.

**Traumatic Genu Recurvatum.**—DAVID TREVOR, M.S.

J. M., female.

First seen in 1946, aged 17, with history of the left knee having been struck with a hockey stick five years previously. After two days' rest in bed the symptoms of pain and swelling in the knee cleared up and no further trouble was experienced until about the middle of 1946 when the knee repeatedly gave way and "locked" in a bent position. Abnormalities detected on examination were: (1) Hyperextension of the knee-joint of 45 degrees compared with a hyperextension of the right knee of 10 degrees. (2) About 1 in. shortening of the limb, partly in the tibia and partly in the femur. (3) Mild degree of lateral and antero-posterior laxity of left knee.



FIG. 1.



FIG. 2.



FIG. 3.

FIG. 1.—Right knee 10 degrees hyperextension.

FIG. 2.—Left knee. 45 degrees hyperextension; lack of development of femoral condyles anteriorly, allowing the excessive degree of hyperextension.

FIG. 3.—Left knee after operation. With the knee fully extended the amount of hyperextension is the same as the right knee; osteotomy site and wedge bone graft from iliac crest well healed; screw was used to hold the tibial tubercle with the attached patellar tendon in position.

Diagnosis of traumatic genu recurvatum was made, due to lack of development of the femoral condyle, anteriorly, caused by the injury five years previously.

March 1948: A wedge osteotomy of the upper end of tibia with bone graft from the iliac crest. The patellar tendon with a portion of the tubercle of the tibia was reflected upwards, as the osteotomy site was at this level. The tubercle was replaced and fixed in position by one screw. Knee-joint immobilized in plaster for several weeks until sound union of graft had occurred at the osteotomy site.

When seen recently the excessive hyperextension of the knee-joint was corrected, there being about 10 degrees of hyperextension. Some laxity laterally and antero-posteriorly remained but this was well controlled by quadriceps activity. Flexion of knee-joint had full range. Patient stated that she could do anything she wanted with the knee and that it gave rise to no symptoms whatsoever.

**Congenital Deformity of Wrists.**—R. C. F. CATTERALL, F.R.C.S.

G. A., male, aged 13 months.

Has attended hospital since age of 3 months on account of congenital deformity of wrists. Treatment was at first deferred pending resolution of gastro-enteritis.

When first examined he was a healthy-looking child, with gross deformity of forearms so that the thumbs lay comfortably against the medial humeral epicondyles. The hands as such were within normal limits (fig. 1).



FIG. 1.—Without appliances. Note prehensile index fingers.



FIG. 2.—Wearing appliance on left forearm.

X-rays: Complete absence of both radii; remainder of skeleton normal.

He has been treated by manipulations of the wrists to correct the deformity followed by immobilization first in plaster of Paris and later in small spring-loaded aluminium splints (fig. 2.) Some degree of correction has been attained and it is suggested that some light splinting should be continued until the time comes for arthrodesis of both wrists at the age of 7 or 8 years.

**Neuropathic Joint Showing a Fracture of the Lower End of the Right Femur and Internal Condyle of the Right Tibia Both Involving the Knee-joint.**—W. E. TUCKER, M.B.E., F.R.C.S.

J. G., male, aged 65.

The patient first noticed the swelling in the right knee about October 1946 which gradually increased. There was no history of injury and, although there was some aching, pain was not a marked feature.

He was given diathermy for synovitis of the right knee but the knee became very unstable.

In April 1948 radiographs were taken and the swelling diagnosed as a sarcoma of the lower end of the femur.



FIG. 1.—Antero-posterior view of right knee and lower end of femur taken on 14.10.48, two years after the onset of symptoms.

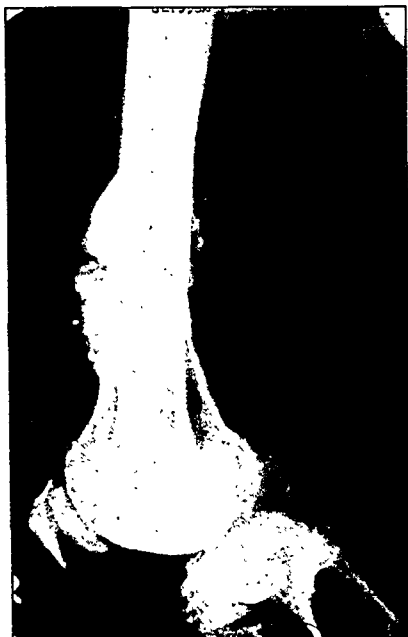


FIG. 2.—Lateral view of the right knee taken on the same day. This shows marked periosteal reaction of the lower third of the femur.

He attended my Out-patients first on May 25, 1948. There was a large painless swelling involving the lower third of the right femur and knee-joint, which was hard and bony on the inner side of the lower end of the femur. The knee-joint was very unstable with marked wasting of the quadriceps. Radiographs revealed a split fracture of the lower third of the femur and internal tibial condyle both involving the knee-joint (*see* figs. 1 and 2).

Blood and C.S.F. tests: The Wassermann reaction was negative and all components normal.

Neurological tests showed diminished knee and ankle jerks with impaired sensation in both lower extremities.

The condition was diagnosed as a Charcot's joint due to tabes dorsalis.

The knee was supported, given intensive physical treatment, chiefly faradism, and has become symptom-free. The patient can now walk comfortably with the aid of a stick.

#### Spondylolisthesis with Bilateral Drop Foot.—G. P. ARDEN, F.R.C.S.

Male patient, aged 79.

Noticed that he had bilateral drop foot for several months. No pain. No history of injury.

*On examination.*—Bilateral weakness of the anterior tibialis and peronei muscles. Both knee and ankle jerks absent. Superficial and deep sensation is also partly lost in both feet. Anal reflex absent. P.R.: Enlarged prostate with a large nodule on the right side.

*Investigations.*—W.R. negative. Kahn negative. Serum acid phosphatase 1.6 units.

*X-ray report* (12.11.48).—Gross osteo-arthritic changes of lumbar spine. Spondylolisthesis L.4 and L.5. Narrowing and deformity of L.5 with marked loss of joint



FIG. 1.—A. P. view showing osteo-arthritic changes affecting L. 3, 4 and 5, and sacralization of L. 5.



FIG. 2.—Lateral view showing spondylolisthesis between L. 4 and 5, with narrowing of this disc. Secondary osteo-arthritic changes also present.

space L.4 and L.5. L.5 and S.1 joint is also narrowed (figs. 1 and 2). Gross osteo-arthritic changes carpometaacarpal joint left thumb. Minimal changes of other bones of hand and wrist.

*Treatment.*—Bilateral toe-raising springs.



## Section of Neurology

President—WILLIAM JOHNSON, M.C., M.D., F.R.C.P.

[March 3, 1949]

### Traumatic Changes in the Brain after Spontaneous Delivery at Full Term

By Professor B. BROUWER (*Amsterdam*)

It is well known that various clinical syndromes may arise in infants after birth in which artificial aid has been given, for example, facial nerve palsy, hemiplegia, dystocia with spinal paralysis and mental disorders, especially idiocy. Aschhoff, however, pointed out that hæmorrhages in the pia-arachnoid and in the central nervous system may occur in almost every birth. It depends on their extension and localization whether these will disappear totally, without clinical defects. It is true that blood is frequently present in lumbar punctures in the first few days after birth and retinal hæmorrhages may also occur. These may be absorbed later on. In 1927 Schwartz published his, now famous, article on the traumatic lesions in the central nervous system at birth and with his co-workers of the Frankfurt school he gave a careful description of the various changes in such brains. Their investigations have shown that destructive processes in the central nervous system may not only occur in premature infants but also in babies after normal delivery at term. Anatomical examination of cases of birth injury shows that not only are hæmorrhages in various parts of the central nervous system frequent, but that other destructive processes (encephalomalacia, formation of cavities, &c.) also occur, especially in the areas of the brain from which the venous blood flows into the vena magna Galeni.

Kinnier Wilson (1940) stated that many problems regarding the connexion between birth injury and clinical syndromes have not been completely solved.

During the last two years the Central Institute for Brain Research at Amsterdam received the brains of 6 children in which signs of birth injuries were found, although these children were full-term and had been delivered without artificial aid. The material was studied in co-operation with Dr. C. de Lange, former Professor of Pædiatrics in the University of Amsterdam. Four of these brains were investigated microscopically by Professor de Lange and myself, and we are still engaged on two others. In one of these, Case I, serial sections through various parts of the brain were made. I will start my demonstration with this case.

*CASE I.—Microcephaly with Subdural Hæmatoma in the Parietal Region of Both Sides.*

Female. Normal, full-term delivery on November 29, 1945. Birth weight was 3,530 grammes. For some days the child was cyanosed, she had convulsions and the breathing was irregular. She was treated in hospital with oxygen and injections. X-rays of the skull revealed that the anterior fontanelle was small, the coronal sutures were almost invisible but the occipital sutures were wide. After a short time the child's condition improved and she was sent home. At the age of 2 months there were clonic contractions of the right arm and later of the muscles of the eyeballs and of other parts of the body. At the age of 5 months the child was readmitted to hospital. She was now a microcephalic idiot. She suffered from frequent epileptic fits, but was not paralysed. The knee-jerks were increased. There were no retinal changes. The radiological examination revealed the microcephaly but the base of the skull was normal. She did not react to light but slightly to acoustic stimuli. There was no spontaneous nystagmus, but now and then convergent strabismus. There were no signs of meningitis, the arm reflexes were normal, the knee-jerks increased. The right frontal bone was trephined, but the child died some hours later.

*Post-mortem (Professor H. T. Deelman).—A subdural hæmatoma in the parietal region of both sides was found. There was microcephaly with polygyria but no real congenital microgyria (figs. 1 and 2). The internal organs did not show any signs of congenital malformation. The weight of the cerebrum was 345 grammes. After cutting the brain in a frontal plane a marked reduction of the centrum semi-ovale was seen. This centrum and the cortex showed a slightly yellow colour.*

*Histology (The Institute).—The pia-arachnoid contained many cells, but perivascular infiltrations were not present and there was no real leptomeningitis. Some parts of the cerebral cortex were normal, but most of it was damaged. In the lateral part of the occipital lobe, for example, the cyto-architectonic structure was totally disturbed. Many cells and fibres were degenerated. In the*

white substance of the gyri many cells contained fat. In the cortex itself fat cells were also present filling up the walls of the blood-vessels or forming conglomerations in which the remnants of blood-vessels were visible. In several places these conglomerations were changed into so-called "pori", when the cells, filled up with lipoid substance, have been transported to the venous sinus. Now and then fat cells were seen in these pori. Fibrillar glia and astrocytes were present. Many portions of cerebral tissue were apparently isolated from the adjacent parts of the cortex. They were surrounded by a

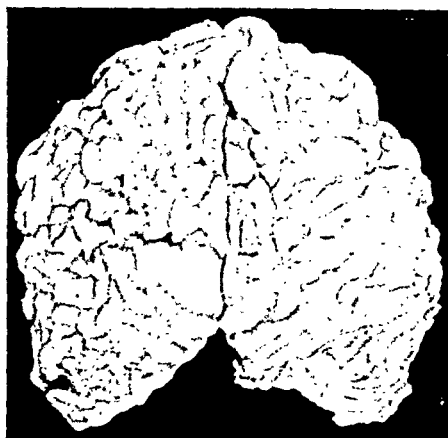


FIG. 1 (Case I).—Microcephalia and polygyria.

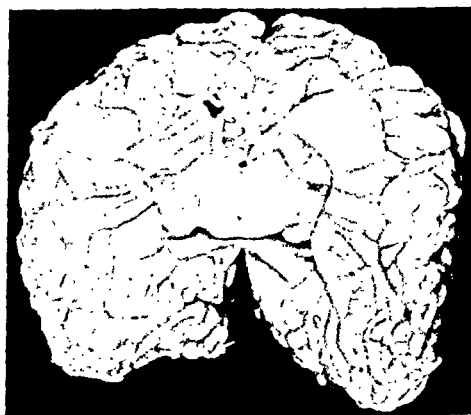


FIG. 2 (Case I).—Microcephalia and polygyria.

small layer of connective tissue originating from the wall of a blood-vessel. In various places such isolated pieces were lying together, giving the impression of a "cactus-formation" (fig. 3). In these isolated pieces chiefly neuroglia and blood-vessels were seen.

Changes of similar intensity were seen in other parts of the cortex, but in many of these sections the pathological process was less pronounced. Usually a fibrillar gliosis was visible in the three upper layers of the cortex. As a rule several ganglion cells in deeper layers were still unimpaired, for example



FIG. 3.

FIG. 3 (Case I).—"Cactus" formation in the cortex. (Nissl preparation.)



FIG. 4.

FIG. 4 (Case I).—Section at the level of the beginning of the neo-thalamus, stained after Weigert-Pal. Figs. 1, 2, 3 and 4 are reproduced from *Koninklijke Nederlandsche Akademie van Wetenschappen (Proceedings)*, 1948.

in the left motor area. The paraffin sections of the striate body and the cerebellum did not show any alterations. The sections of the medulla through the level of the maximal development of the inferior olives might be regarded as normal. The pyramidal tracts for instance were well formed, showing myelinization in accordance with the age of the child.

Serial sections were made through the striate bodies, the optic thalamus with the surrounding pallium. The left half of the cerebrum was alternatively stained with Weigert-Pal and van Gieson,

the right half with Nissl and here and there with hæmatoxylin-eosin. Further serial sections were made through the right occipital lobe and stained after Nissl. The cerebrum was very small, but there are no grounds for the assumption of a general or local congenital disturbance in development. There was, for instance, no heterotopia, so frequently seen in microcephaly, neither was any evidence of an encephalitis found. The primary destruction was seen only in the pallium, not in the deeper structures of the brain (fig. 4). Chiefly the dorsal and lateral parts of the neopallium were affected. The archipallium and the palæopallium were normal. The centrum semi-ovale was reduced in size by loss of many fibres. The corpus callosum was small and showed secondary degeneration of fibres. Of the deeper situated parts of the brain it might be stated that the striate bodies, the hypo-, epi- and sub-thalamus, the capsula interna and the region of the nucleus ruber were unchanged. In the neo-thalamus the medial nucleus, the dorsolateral nucleus and the pulvinar showed retrograde degeneration of cells with secondary increase of glia in many places. The other thalamic nuclei might be regarded as normal.

From this demonstration it will be clear that several pathological changes must be regarded as the direct consequence of the traumatic action with asphyxia at birth. This trauma must have been rather severe, as is proved by the existence of the subdural hæmatoma in both parietal regions. The alterations, however, were not limited to the parietal regions, but extended much further over the hemispheres.

The polygyria and microgyria were not caused by a congenital malformation, for destruction and shrinking of the various layers of the cortex were found with secondary increase of neuroglia. In actual congenital microgyria, caused by a pathological development of the various cellular layers of the cortex, such shrinking is not seen.

The question arises whether the microcephaly may also be regarded as the result of the trauma at birth, because usually this abnormality is the result of arrest of cerebral development and of pathological processes during the foetal life. I refer, for example, to the study of Greenfield and Wolfsohn (1935), in which two different forms of microcephalia vera, the agyric and the complex microgyric types, are described. In these brains several symptoms of malformation, especially heterotopia, were found. The fact that in our case the systematic examination of the brain in serial sections did not show any symptom of real malformation is a strong argument for the conception that here the microcephaly was of traumatic origin.

In his investigations on malformations of the brain Anton (1904) found that in microcephaly the projection fibres are frequently less involved in the process than the associative elements. Such a contrast is also plain in our observation. The pyramidal tracts and various neo-thalamic nuclei were not degenerated. We have dealt elsewhere with this question (Brouwer and de Lange, 1948).

CASE II.—*Clinical Diagnosis: Congenital Meningitis. Pathology: Traumatic Hæmorrhage in the Right Occipital Ventricle.*

In this case, which was also spontaneously born at term, convulsions were seen from the beginning. The child was taken into the hospital with her mother, because the latter had complete rupture of the perineum. The child's head was retracted and the legs crossed. The day after admission gangrene and bullæ appeared on the legs and the arms. At lumbar puncture the amount of protein in the spinal fluid was a little too high and several erythrocytes were found. Gradually the condition worsened. The child did not take food and was unconscious. Death occurred on the 13th day after birth.

*Post-mortem.*—No alterations of importance were found in the internal organs. In the right posterior horn there was a blood clot, the size of a peanut (fig. 5). At the microscopical examination the pia-arachnoid contained a considerable number of mononuclear cells, but no polynuclear leucocytes were found and no cuffs round the vessels. At some spots hæmorrhages were visible. The blood clot in the posterior horn contained pigment and showed already the beginning of organization. The architectonic of the various parts of the cortex was preserved. In several places calcified ganglion cells were found. Small conglomerations of glial cells were seen throughout the tissue round the ventricle, also amœboid glia in the white substance. All over the brain dilated and hyperæmic vessels, especially smaller veins, were seen. The hæmorrhage in the right ventricle explains the convulsions and the widespread disturbance in the circulation caused death.



FIG. 5 (Case II).—Blood clot in the right posterior horn. (Nissl preparation.)

**CASE III.—Underdevelopment of the Brain with Traumatic Polygyria and Severe Destruction of the Cortex.**

Normal delivery. Information about the first days of the child's life was not available. The first pathological symptoms appeared three months after birth. The child was taken into hospital, because it became ill with fever and slight diarrhoea. Shortly after admission convulsions occurred and all the extremities were spastic. The child was anæmic, the number of erythrocytes was only 2,200,000. The consulting neurologist suggested the possibility of a lesion of the brain-stem. Albumin was found in the urine. At the age of 13 months the child was readmitted to hospital. According to information the rigidity had lessened at home and the fits disappeared after prescription of luminal. But gradually the general condition was getting worse. The patient was spastic and apathetic. The urine contained albumin and a large number of leucocytes. At lumbar puncture nothing abnormal was found. The child died after some days at the age of 13 months with the symptoms of hypothermia and irregular breathing.

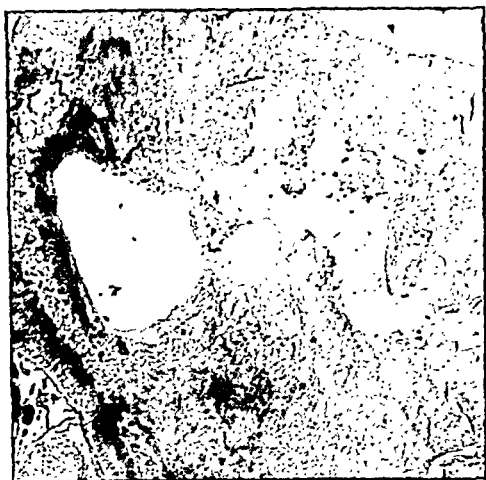


FIG. 6 (Case III).—"Pori" (cavities) in different stages of development. (Stained with hæmatoxylin-eosin.)

**CASE IV.—Traumatic Malacia in the Left Parietal Lobe, to a Less Extent Also in the Right Side.**

This case was seen by me in consultation. The patient was the second child of healthy parents. The baby was full term but labour was precipitate and the mother had a rupture of the perineum. The child appeared normal, but developed epileptic fits at 7½ months, when he was admitted to hospital. There was a slight increase of temperature but no objective neurological symptoms were found and the retina was normal. Lumbar puncture gave a clear fluid, there was no pleocytosis and no increase of protein. The culture proved to be sterile. Encephalitis was diagnosed and penicillin

was given. After some weeks the temperature was normal and the fits disappeared, but the child was lethargic, waking only when being fed. The lethargy gradually subsided, but the fits reappeared. The patient died at the age of 2 years and 4 months; the clinical picture was that of an acute disease with fits and high temperature.

The whole clinical history will be described by Professor de Lange elsewhere.

**Post-mortem** (Dr. O. H. Dijkstra).—General thrombosis of the sinuses of the brain. There was pus in both middle ears. This explained the final extensive sinus thrombosis. But we found in the left parietal lobe an old focus of malacia extending from the cortex into the white substance of the centrum semi-ovale (fig. 7), the latter having also a yellowish tinge. The focus spread frontally into the sensorimotor region. In the dorsal part of the right parietal lobe a similar focus was seen but of less extent.

**Histology.**—Much of the cortex in the left superior parietal lobe was destroyed. Here and there the so-called hollow gyri were seen. There were also many calcified ganglion cells. The leptomeninges and the damaged brain tissue showed a large number of lipid cells. The white substance of the cortex was also destroyed here and contained numerous "Körnchenzellen" and macrophages. Less



FIG. 7 (Case IV).—Malacia in the left parietal lobe.

intensive changes were also seen in the right parietal lobe. These older foci bore the typical signs of a birth injury.

It is true that the epileptic fits did not start before the age of 7½ months. It is, however, well known that in many cases these fits do start after a silent period. Recently Penfield and Steelman (1947) reported on 76 cases of focal epilepsy. The cause of the original lesion in their series was most often head injury, secondly birth injury and thirdly local infection. When the cause was birth injury the onset of the seizures was delayed. The authors did not see attacks in the first year of life and 82% of the patients had their first seizure after the age of 5 years. In several of their cases a local microgyria was revealed at operation, in which the number of ganglion cells within the cortex was greatly reduced.

I shall briefly mention our two final specimens. The first (Case V) was a child born in Indonesia. The birth was spontaneous but difficult. The child was asphyctic, with epileptic fits immediately after birth. He was brought to Holland and admitted



FIG. 8 (Case V).—Several small cavities on both sides.



FIG. 9 (Case V).—Traumatic cavity in the cortex cerebri. (Nissl preparation.)

to our Hospital for Children's Diseases. There was hypertonia of the extremities with increased reflexes. The retina was normal and lumbar puncture revealed no abnormalities. The child died at the age of 7 months.

*Post-mortem.*—Microcephaly with microgyria in the region of the sensorimotor area on both sides. A frontal section through the brain showed many small pori (fig. 8), and the brain tissue was yellowish.

*Histology.*—The pori showed the typical picture as seen in birth injury (fig. 9). In some of them the damaged brain tissue could still be seen. The Sudan-stained sections showed an accumulation of fat cells. The changes were not limited to the sensorimotor area but extended also into the frontal and parietal lobes.

In the last case (VI) delivery was spontaneous and at term; the child was cyanosed after birth. It developed a severe icterus but no real neurological symptoms and no epileptic fits. The child died at the age of 4 weeks and at the post-mortem examination an extensive hæmorrhage was found over a great part of the right hemisphere and the medial side of the left one. Also at the base of the brain much blood was found over the temporal lobes.

#### DISCUSSION

It is not well known that a normal delivery may give rise to a serious birth injury. The appearance of convulsive seizures with symptoms of asphyxia is suspect for such a lesion, but this is not always so. Often a period of several months follows after birth before more serious symptoms appear, as I mentioned already in the description of our fourth case. There is no special clinical picture which is reliable in establishing the diagnosis.

Ingraham and Matson (1944) writing on subdural hæmatoma in infancy ascribed 28 cases to a severe trauma of birth. They recorded as common physical findings convulsions, vomiting, hyper-irritability, stupor and susceptibility to infections. X-ray pictures are necessary, of course, but fractures of the skull are often missing. Therefore

they puncture the subdural space in the frontal suture line beyond the anterior fontanelle. This puncture often makes the diagnosis possible. Not seldom the subdural hæmorrhage is bilateral, just as in our first case. In a later period the neurological syndrome also shows after their experience many variations, as spastic paresis of one or both sides, changes in the retina, mental retardation, &c.

As to the pathogenesis of the lesion of the brain at delivery we may conclude the following. Compression of the head by the contractions of the uterus may cause a general shift of the intracranial contents and rupture of the delicate bridging veins. Schwartz explains many of these lesions by the difference of pressure between the inner side of the uterus and the outer world, which pressure is suddenly altered by the delivery. The asphyxia is chiefly caused by the stowage in the veins. Now and then also general causes may have an influence, as for example vitamin-K deficiency.

In the pathological pictures it is surprising to see that the alterations of the cortex often spread much further over the hemispheres than the area of the local injury. Schwartz (1927) already mentioned the fact, that often more recent changes may be found amongst the older lesions in the cortex. Wohlwill (1936) pointed out that in these cerebra many disturbances in the circulation arise owing to traumatic alterations in the innervation of the walls of the blood-vessels, causing insufficient nourishment of the brain tissue, resulting in degeneration. Furthermore the normal and pathological stimuli of the extra-uterine life have an additional destructive influence on such processes, where once the neurovascular apparatus has been damaged.

Finally the question arises whether therapy in these children may be successful. It is proved that repeated spinal punctures are not sufficient and also that the results of treatment with vitamin K are very doubtful.

When the diagnosis of a subdural hæmatoma is made, removal of the blood clot by the neurosurgeon seems indicated, but—as Naffziger and Brown (1934) pointed out—sudden release of the contents of the subdural hæmatoma sacs with resulting alteration in the intracranial pressure relationships is not tolerated well by infants. It may give rise to an acute cerebral œdema, which can be fatal. Therefore Ingraham and Matson (1944) induced the combination of early conservative and ultimate radical treatment of these lesions. They repeat the subdural taps in the frontal suture line regularly, over periods of as long as three weeks, if necessary on both sides. In their experience most of these infants improve rapidly. The next stage in treatment can then be carried out. In all cases where excessive subdural fluid has been demonstrated by these taps, bilateral trephination is carried out by a small burr hole in the temporal region. About one-third of their patients did well with repeated subdural taps and membranes of a subdural hæmorrhage were not established in this group. If the presence of such a membrane has been diagnosed, a fronto-temporo-parietal osteoplastic bone flap is elevated and the solid clot is removed. In their experience the results have sufficiently improved the outlook for the children with a subdural hæmatoma.

In birth injury an early diagnosis is necessary, because otherwise irreparable alterations in the brain, as shown in our observations, make restoration of function impossible. I hope by my lecture to stimulate neurologists to focus their attention on these cases, because I am convinced that many defective neurological conditions are not endogenous but caused by birth.

#### BIBLIOGRAPHY

- ANTON, G. (1904) *Handbuch der pathologischen Anatomie des Nervensystems*. Eds.-Flatau, Jacobsohn und Minor. Berlin.  
 BROUWER, B., and DE LANGE, C. (1948) *Proc. Koninkl. Neder. Akad. van Wetenschappen*, 51, 950.  
 GREENFIELD, J. G., and WOLFSOHN, J. M. (1935) *Arch. Neurol. Psychiat.*, 33, 1296.  
 INGRAHAM, F. D., and MATSON, D. D. (1944) *J. Pediat.*, 24, 1.  
 NAFZIGER, H. C., and BROWN, H. A. (1934) *Surg. Clin. N. Amer.*, 14, 1465.  
 PENFIELD, W., and STEELMAN, H. (1947) *Ann. Surg.*, 126, 740.  
 SCHWARTZ, P. (1927) *Ergebn. inn. Med. Kinderheilk.*, 31, 165.  
 WILSON, S. A. K. (1940) *Textbook of Neurology*. London.  
 WOHLWILL, F. (1936) *Cerebrale Kinderlähmung*. *Handbuch der Neurologie*, 16, 35. Eds.—  
 Bumke and Foerster.

Dr. N. G. Hulbert, Dr. W. G. Wyllie, Dr. R. M. Norman and Dr. Dermot MacCarthy took part in the subsequent discussion.

## Section of Ophthalmology

President—CHARLES GOULDEN, O.B.E., M.A., M.D., F.R.C.S.

[November 5, 1948]

### Anterior Retinal Dialysis

By C. DEE SHAPLAND, F.R.C.S.

THE term "disinsertion" of the retina was coined by Gonin to describe the festoon-shaped ruptures in that membrane which occur at the extreme periphery of the fundus, are not infrequently associated with trauma and are apparently the result of a tearing away of the retina at its relatively thin attachment at the ora serrata. The term was perhaps a little unfortunate as the retina can hardly be regarded as being inserted into the ciliary body at the ora serrata since the two layers of the secondary optic vesicle are continued forwards as the ciliary epithelium and ectodermal portion of the iris. Hence it was soon replaced by the more appropriate appellation "anterior retinal dialysis".

*The incidence of retinal detachment with peripheral dialysis.*—In the first 100 cases of retinal detachment which I investigated there were 37 with an anterior retinal dialysis [1] and in the second 100 cases 25 [2]; in a further series of 140 cases the percentage was 30.7 [3], and in my own series of 155 cases (164 eyes) the percentage is 33.5 [6]. In approximately one-third of all cases of retinal detachment, therefore, one may expect to find it associated with the anterior retinal dialysis.

*Types of anterior retinal dialysis.*—Peripheral dialyses would appear to be of four types as regards their pathogenesis. By far the commonest are those situated in the lower temporal quadrant of an eye which is hypermetropic, emmetropic or has but a low degree of myopia; trauma figures in about 39% of cases and almost certainly results from peripheral cystic degeneration of the retina. A second type is that seen after severe direct trauma to a previously healthy eye, usually a concussion injury from an arrow or air-gun pellet; these seem to favour the upper temporal quadrant of the globe but are probably always in the immediate vicinity of the site of impact of the missile. Traction dialyses due to the retraction of scar tissue make a third type—these were not infrequently seen as a complication of Gonin's operation of igni-puncture, they also occur in advanced cyclitis following the organization of shrinking cyclitic exudates and they are occasionally met with after a perforating

they puncture the subdural space in the frontal suture line beyond the anterior fontanelle. This puncture often makes the diagnosis possible. Not seldom the subdural hæmorrhage is bilateral, just as in our first case. In a later period the neurological syndrome also shows after their experience many variations, as spastic paresis of one or both sides, changes in the retina, mental retardation, &c.

As to the pathogenesis of the lesion of the brain at delivery we may conclude the following. Compression of the head by the contractions of the uterus may cause a general shift of the intracranial contents and rupture of the delicate bridging veins. Schwartz explains many of these lesions by the difference of pressure between the inner side of the uterus and the outer world, which pressure is suddenly altered by the delivery. The asphyxia is chiefly caused by the stowage in the veins. Now and then also general causes may have an influence, as for example vitamin-K deficiency.

In the pathological pictures it is surprising to see that the alterations of the cortex often spread much further over the hemispheres than the area of the local injury. Schwartz (1927) already mentioned the fact, that often more recent changes may be found amongst the older lesions in the cortex. Wohlwill (1936) pointed out that in these cerebra many disturbances in the circulation arise owing to traumatic alterations in the innervation of the walls of the blood-vessels, causing insufficient nourishment of the brain tissue, resulting in degeneration. Furthermore the normal and pathological stimuli of the extra-uterine life have an additional destructive influence on such processes, where once the neurovascular apparatus has been damaged.

Finally the question arises whether therapy in these children may be successful. It is proved that repeated spinal punctures are not sufficient and also that the results of treatment with vitamin K are very doubtful.

When the diagnosis of a subdural hæmatoma is made, removal of the blood clot by the neurosurgeon seems indicated, but—as Naffziger and Brown (1934) pointed out—sudden release of the contents of the subdural hæmatoma sacs with resulting alteration in the intracranial pressure relationships is not tolerated well by infants. It may give rise to an acute cerebral œdema, which can be fatal. Therefore Ingraham and Matson (1944) induced the combination of early conservative and ultimate radical treatment of these lesions. They repeat the subdural taps in the frontal suture line regularly, over periods of as long as three weeks, if necessary on both sides. In their experience most of these infants improve rapidly. The next stage in treatment can then be carried out. In all cases where excessive subdural fluid has been demonstrated by these taps, bilateral trephination is carried out by a small burr hole in the temporal region. About one-third of their patients did well with repeated subdural taps and membranes of a subdural hæmorrhage were not established in this group. If the presence of such a membrane has been diagnosed, a fronto-temporo-parietal osteoplastic bone flap is elevated and the solid clot is removed. In their experience the results have sufficiently improved the outlook for the children with a subdural hæmatoma.

In birth injury an early diagnosis is necessary, because otherwise irreparable alterations in the brain, as shown in our observations, make restoration of function impossible. I hope by my lecture to stimulate neurologists to focus their attention on these cases, because I am convinced that many defective neurological conditions are not endogenous but caused by birth.

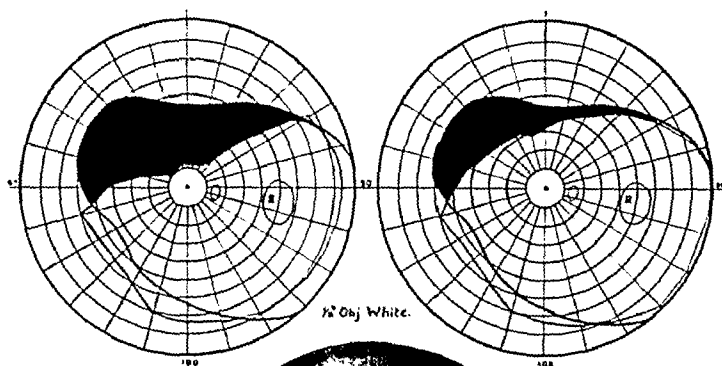
#### BIBLIOGRAPHY

- ANTON, G. (1904) *Handbuch der pathologischen Anatomie des Nervensystems*. Eds.-Flatau, Jacobsohn und Minor. Berlin.  
 BROUWER, B., and DE LANGE, C. (1948) *Proc. Koninkl. Neder. Akad. van Wetenschappen*, 51, 950.  
 GREENFIELD, J. G., and WOLFSOHN, J. M. (1935) *Arch. Neurol. Psychiat.*, 33, 1296.  
 INGRAHAM, F. D., and MATSON, D. D. (1944) *J. Pediat.*, 24, 1.  
 NAFFZIGER, H. C., and BROWN, H. A. (1934) *Surg. Clin. N. Amer.*, 14, 1465.  
 PENFIELD, W., and STEELMAN, H. (1947) *Ann. Surg.*, 126, 740.  
 SCHWARTZ, P. (1927) *Ergebn. inn. Med. Kinderheilk.*, 31, 165.  
 WILSON, S. A. K. (1940) *Textbook of Neurology*. London.  
 WOHLWILL, F. (1936) *Cerebrale Kinderlähmung*. *Handbuch der Neurologie*, 16, 35. Eds.—Bumke and Foerster.

Dr. N. G. Hulbert, Dr. W. G. Wyllie, Dr. R. M. Norman and Dr. Dermot MacCarthy took part in the subsequent discussion.

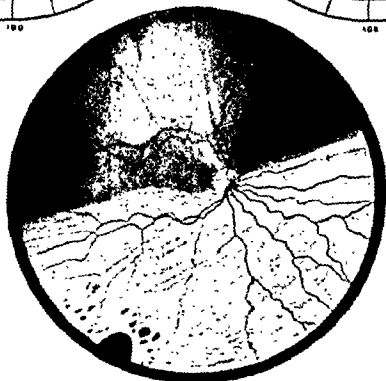


usually rounded or atrophic fenestrated areas of the retina—in a further 11·6% (fig. 2). In my own series of 155 cases [6], the dialyses were multiple in 12·7% and associated with other retinal defects in a further 9·1%. These figures are similar.



Lieut. A. R. Jan. 30, 1945. Field before operation; V. = 6/36.

Lieut. A. R. March 8, 1945. Field after operation; V.  $\bar{c} + 1.0 = 6/6$ .



Lieut. A. R. Inferior detachment showing single dialysis associated with multiple rounded holes.

FIG. 2.

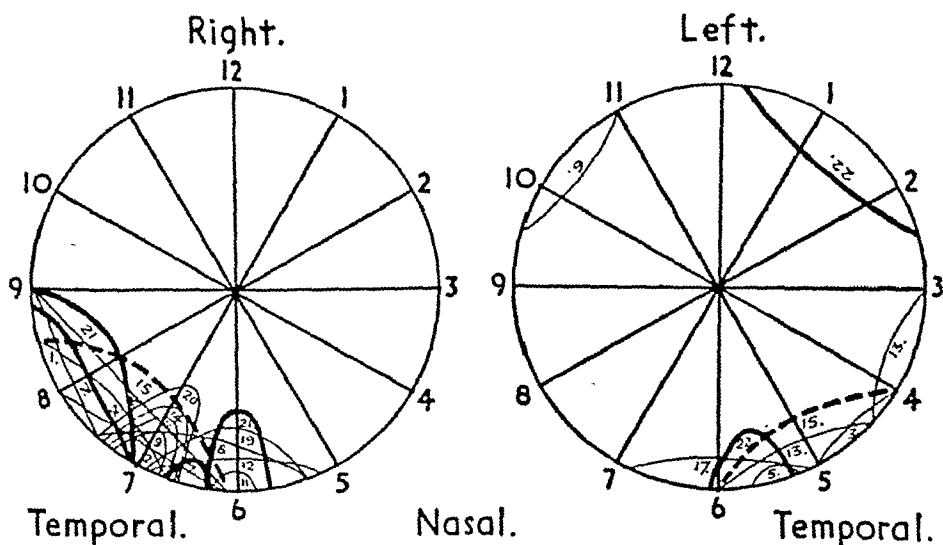
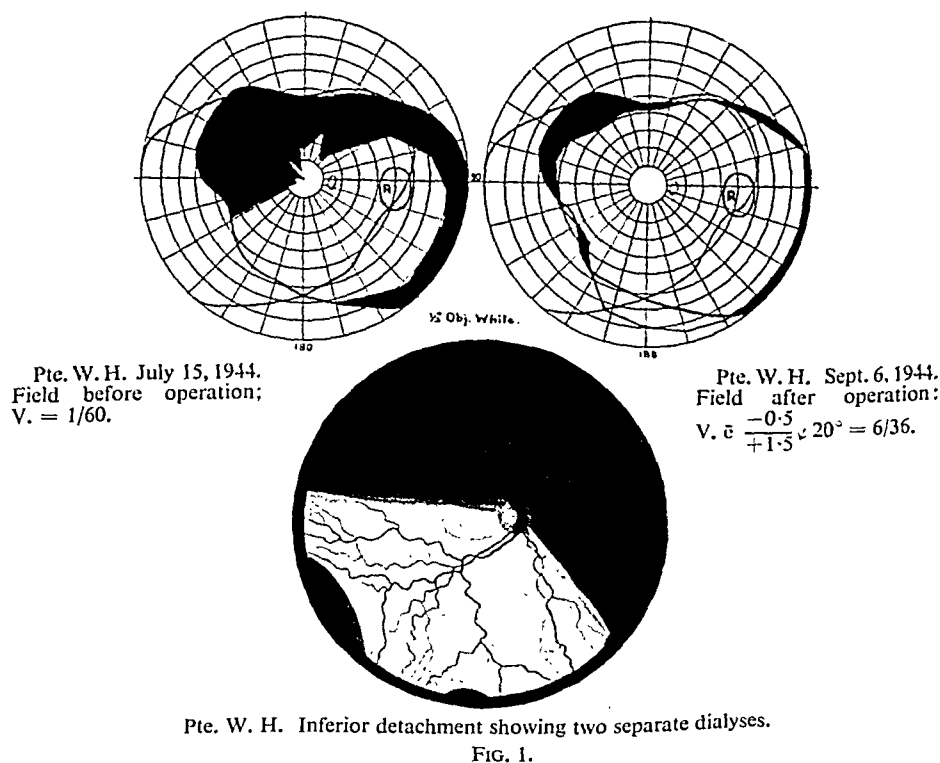


FIG. 3.—Service cases. Distribution of dialyses in 22 eyes. Dialyses multiple in 3 eyes (13·6%) and combined with atrophic fenestrated areas in a further 13·6%. Fine line—single. Heavy black line—multiple. Dotted line—bilateral.

injury. The fourth type comprises the giant dialyses which may extend half-way or more around the circumference of the globe, have apparently no preference as regards location and are usually seen in the highly myopic eye.

*Size of anterior retinal dialyses.*—The anterior retinal dialysis averages about 5 mm. in long axis, that is, it subtends an arc of 30 degrees at the ora serrata. In a series of 425 cases of retinal detachment which I investigated [4], 58.7% of the dialyses present subtended an arc of 30 degrees or less, 25.6% one of from 30 degrees to 60 degrees, 9.1% one of from 60 degrees to 90 degrees and in 4.1% an arc of from 90 degrees to 180 degrees. In two cases of that series the retina of over half the circumference of the globe at the ora serrata was torn away and it is in such cases, especially when the dialysis is above, that the rare condition of reflection of the retina is observed, the upper half of the retina gravitating down upon the lower so that the outer surface of the detached retina is seen through the pupil below and the exposed choroid above. The most extreme degree possible—that of total anterior retinal dialysis in which the entire circumference of the retina at the ora serrata is separated—I have observed only once, and this was in one of my Service cases in whom the retina was retracted into a shrunken globular mass resembling a tumour on the optic disc.

Dialyses are not infrequently multiple but are usually in close proximity (fig. 1),



occasionally, however, they may be widely separated and the unusual appearance of two separate retinal detachments in a single eye may then be presented. This is quite rare, however, and I have only observed it twice.

In a series of 140 cases of retinal detachment [3], the dialyses present were multiple and adjacent in 9.3% of their incidence and combined with other holes

where the vitreous framework has its fullest development and its firmest anchorage, and where the mode of apposition of the two layers of the secondary optic vesicle suddenly alters, the loose relationship between the retina and the pigment epithelium giving place abruptly to the firm fusion of the two layers of the ciliary epithelium.

In the still larger proportion of cases in which no history of injury can be obtained additional factors must be sought. The periphery of the retina is thinnest on the temporal side and it is here that the retina is earliest affected by peripheral cystic degeneration. In my experience large retinal cysts definitely favour the periphery of the infero-temporal quadrant of the globe (fig. 5) and there is a distinct tendency for such

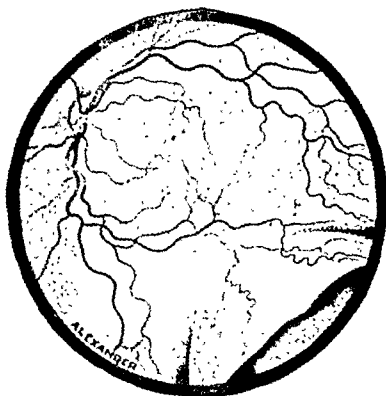


FIG. 5.—Rupture of peripheral retinal cyst with consequent dialysis.

to occur bilaterally. This observation must be correlated with the not infrequent occurrence of bilateral symmetrical retinal detachments [5] which form about 2% of any large series of detachment cases (fig. 6), and in which the detachment starts

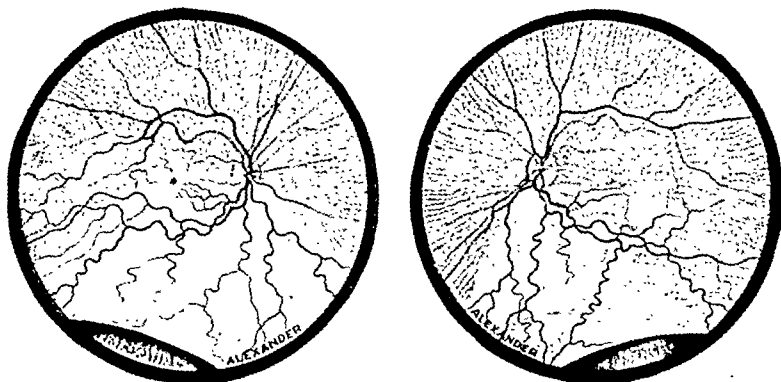


FIG. 6.—Showing typical bilateral symmetrical detachment of retina in relation to symmetrically placed dialyses infero-temporally.

around symmetrically placed dialyses almost invariably situated infero-temporally and in which it is quite exceptional to obtain any history of injury. A developmental anomaly with cystic formation would appear to be the basis of both these types of case.

*Operative results.*—There is very general agreement that a retinal detachment associated with an anterior retinal dialysis has the best operative prognosis. This

Thus anterior retinal dialyses may be expected to be multiple and adjacent in about 11% of their incidence and associated with other retinal defects in about 10%.

*Location of the anterior retinal dialysis.*—The anterior retinal dialysis favours the lower half of the globe and especially its inferior temporal quadrant (fig. 3). Thus in the series of 425 cases [4] 73.5% of the dialyses present were located here, in a further series of 140 cases, 81.4% of the retinal dialyses were so situated, whilst in my Service series of 33 cases no less than 90% of the dialyses were in the lower temporal quadrant of the globe.

The anterior retinal dialysis favours the hypermetropic or emmetropic eye or that with but a low degree of myopia. This is well shown in fig. 4, from which it is clear that

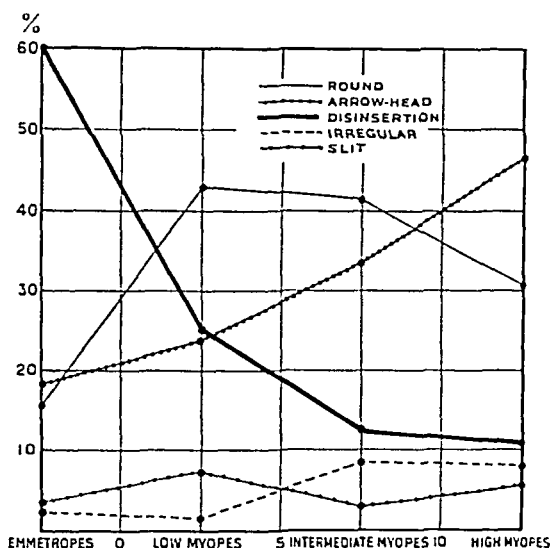


FIG. 4.—Diagram showing the incidence of the five types of retinal hole in the refractive groups in a series of 425 cases. (From *Brit. J. Ophthalm.*, 1934, 18, 7.)

the peripheral dialyses, forming some 60% of the tears present in the hypermetropic or emmetropic eye, fall as the measure of myopia increases until in the group of high myopes (over 10 D) their incidence has fallen to only 10.8%, and these are often giant dialyses. This is also well demonstrated in my series of 155 cases (164 eyes) [6].

|                     | Emm.-Hyp. | Myopia<br>0-5D | Myopia<br>5-10D | Myopia<br>over 10D | Aphakia |
|---------------------|-----------|----------------|-----------------|--------------------|---------|
| Eyes                | 60        | 34             | 32              | 27                 | 11      |
| Peripheral dialyses | 55.0%     | 38.2%          | 6.2%            | 11.1%*             | 18.2%   |

\*All these were giant dialyses.

In the series of 425 cases it was found that 70.3% of the anterior retinal dialyses occurred in males and 29.7% in females; the average age was 31.1 years, and 39.0% were associated with a history of trauma (see *Brit. J. Ophthalm.*, 1934, 18, 8, Table II).

It is thus clear that the dialyses occur chiefly in males, at a relatively early age, and that a fairly high percentage are of traumatic origin.

The anterior retinal dialysis, therefore, occurs chiefly in emmetropic eyes and in the infero-temporal quadrant. A history of trauma is obtained in about 39% of the cases having this type of rent. In a proportion of these, no doubt, no factor other than that of direct violence is required, the retina giving way at the point where it is thinnest and most prone to degeneration, where it is unsupported by vessels,

## Section of Experimental Medicine and Therapeutics

President—Professor G. W. PICKERING, M.A., M.B., F.R.C.P.

[March 8, 1949]

### DISCUSSION ON ANTIHISTAMINE DRUGS

Professor W. A. Bain (*University of Leeds*): *The Quantitative Comparison of Histamine Antagonists in Man.*

THIS work, done by a small team<sup>1</sup> at Leeds, is part of a general attempt to apply to pharmacological studies in man methods of a quantitative kind such as have hitherto been applied chiefly to animals and to isolated animal tissues. As a starting-point in this quantitative approach to human pharmacology histamine and the histamine antagonists seemed ideal drugs to use, since histamine produces easily measurable reactions in the most extensive and readily available organ of the body and these reactions, as is well known from much qualitative work, are readily modified by histamine antagonists. A further consideration influencing our choice was the practical desirability of developing methods for assessing the relative merits of antihistaminics: this has now become an urgent practical necessity in view of the bewildering rate at which new drugs of this class are being introduced and the inevitable confusion which this is causing.

Our first task was to determine the dose-effect relationship for histamine when the drug was injected into the skin; and the second to determine in what manner and to what extent this was modified by the oral administration of histamine antagonists. From such observations we were able to devise means for obtaining quantitative comparative information about three of the four most important practical aspects of the actions of these drugs—their relative weight-for-weight potencies, their relative durations of action, and their relative therapeutic efficacies. Only the hyoscine-like side actions were not amenable—or were not subjected—to quantitative study.

Our account is necessarily but a brief summary of what we have done. Results are given mostly as mean values: statistical treatment of the data is omitted and will be presented elsewhere. For information about the various drugs mentioned, and about previous work upon them, the reader is referred to the recent reviews by Halpern (1948) and by Hunter and Dunlop (1948).

*The dose-response curve to intradermal histamine and its modification by histamine antagonists.*—The two experimental facts which form the basis of the subsequent observations are these: First, if graded doses of histamine are given intradermally to any individual, and the areas of the resulting wheals or flares are measured when at their maximum, then the relationship between the logarithm of the dose and the effect is linear over at least a three-hundredfold dose range—usually from 0.01  $\mu$ g. to at least 3.0  $\mu$ g., and in many subjects to as far as 10  $\mu$ g. or more—after which the slope of the graph increases suddenly. Second, after the oral administration of an adequate dose of a histamine antagonist the log-dose response curve to intradermal histamine shifts so that it occupies at any given time a new position such that, in the conditions of our experiments and as far at least as the wheal response is concerned, there is an approximately equal percentage reduction of wheal area for each of the test doses of histamine over the range from about 0.03 to at least 10.0  $\mu$ g.

<sup>1</sup>The Author, with Dr. G. Achari, Dr. J. L. Broadbent, Miss M. Robinson, and Dr. R. P. Warin.  
AUG.—EXP. MED. I

was recognized in the early days of Gonin's cautery puncture—provided the dialysis was not too large—and is clearly shown in my own series of 155 cases:

PERCENTAGE REPOSITIONS CORRELATED WITH THE VARIOUS TYPES OF RETINAL DEFECT  
(Service and Civilian)

|                                                |    |    |    |       |
|------------------------------------------------|----|----|----|-------|
| Peripheral dialyses (excluding giant dialyses) | .. | .. | .. | 83.3% |
| 48 eyes                                        |    |    |    |       |
| Round, oval and fenestrated areas              | .. | .. | .. | 68.6% |
| 35 eyes                                        |    |    |    |       |
| U-shaped and radial slit rents                 | .. | .. | .. | 53.6% |
| 56 eyes                                        |    |    |    |       |
| Giant and irregular (including giant dialyses) | .. | .. | .. | 25.0% |
| 12 eyes                                        |    |    |    |       |
| No holes found                                 | .. | .. | .. | 15.4% |
| 13 eyes                                        |    |    |    |       |

I use the term giant dialysis for one which subtends an arc of over 90 degrees at the ora serrata and therefore exceeds 15.3 mm. in length; such occur chiefly in the highly myopic eye and have no obvious preference for position. Myopic detachments associated with giant dialyses have a very bad prognosis, and the only possible way of obtaining a reposition is by posturing the patient for at least a week in such a position as to allow the retina to fall back against the choroid as much as possible—a procedure which often fails as the vitreous gel has insinuated itself behind the retina through the dialysis—and then at operation to pin the retina from ora to ora along a line which passes sufficiently far posteriorly to bring the diathermy reactions to bear upon retina which is still attached or at any rate in close proximity to the choroid.

#### REFERENCES

- 1 SHAPLAND, C. DEE (1931) *Trans. ophthalm. Soc. U.K.*, 51, 152.
- 2 — (1932) *Trans. ophthalm. Soc. U.K.*, 52, 170.
- 3 — (1933) *Trans. ophthalm. Soc. U.K.*, 53, 127.
- 4 — (1934) *Brit. J. Ophthalm.*, 18, 1.
- 5 — (1932) *Trans. ophthalm. Soc. U.K.*, 52, 181.
- 6 — (1948) *Trans. ophthalm. Soc. U.K.* (in press).

We hope to publish the paper on Anterior Retinal Dialysis read by Professor H. J. M. Weve of Utrecht, in a later issue.

after each injection, transferring to millimetre graph paper, and computing directly. The results were calculated from these measurements.

Phenergan is clearly the most powerful of these drugs and Antistin the least so. Thus, while a 50% reduction of wheal area was produced by about 40 mg. Phenergan, it required 275 mg. Anthisan or 600 mg. Antistin to produce the same mean effect. Furthermore, if

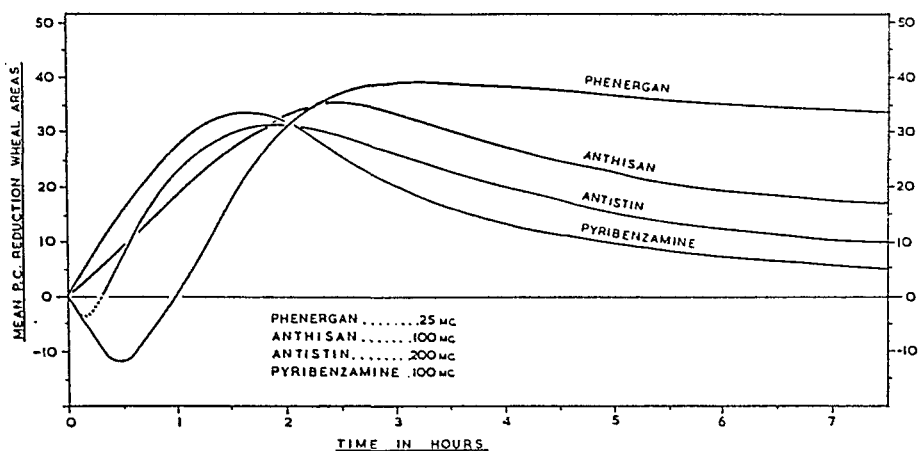


FIG. 2.—To show the variation in the rate of rise and fall of the antihistamine effect of single doses of various histamine antagonists. Mean results from four subjects. Abscissa—time in hours. Ordinate—mean percentage reduction below pre-drug level in wheal areas from intradermal test doses of histamine. The drugs and their doses are indicated on the figure. The individual points from which the graphs are constructed are omitted to avoid confusion.

we assume that the dose-response relationship remains linear throughout its course, then the mean doses of antihistamine theoretically required to abolish the intradermal histamine response are 450 mg. Phenergan, 3,200 mg. Anthisan and 7,000 mg. Antistin respectively—all of them quite intolerable doses.

Such comparisons of relative potency are, of course, facilitated by the fact that the regression lines for the different drugs are parallel, so that there is a simple ratio relating the mean dose of any two antagonists to give equal mean responses. Thus from the results shown in fig. 3 it is evident that about seven times the amount of Anthisan, or fifteen times the amount

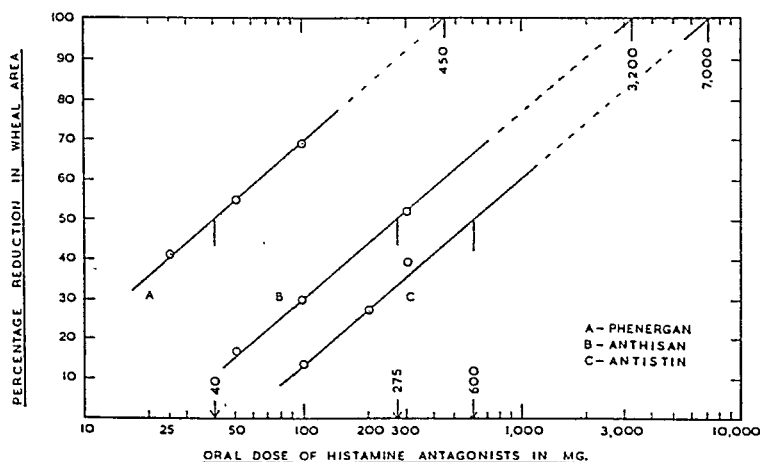


FIG. 3.—To show relationship between dose and maximum antihistamine response for Phenergan, Anthisan and Antistin. Mean results from six subjects. Abscissa—oral dose of drug in mg. on logarithmic scale. Ordinate—mean percentage reduction in wheal areas. Graphs A, B, and C are for Phenergan, Anthisan and Antistin respectively. Mean doses to give 50% reduction in wheal area are indicated on lower abscissa, and theoretical doses to produce 100% reduction on upper abscissa. For further explanation see text.

These facts are illustrated in fig. 1 which shows the mean results from a set of experiments on five subjects. The upper points show the mean wheal areas resulting from the intradermal doses of histamine indicated on the abscissa, and the graph is drawn through these points by eye. The lower points show the corresponding wheal areas three hours after the ingestion of 25 mg. Phenergan (3277 R.P.).

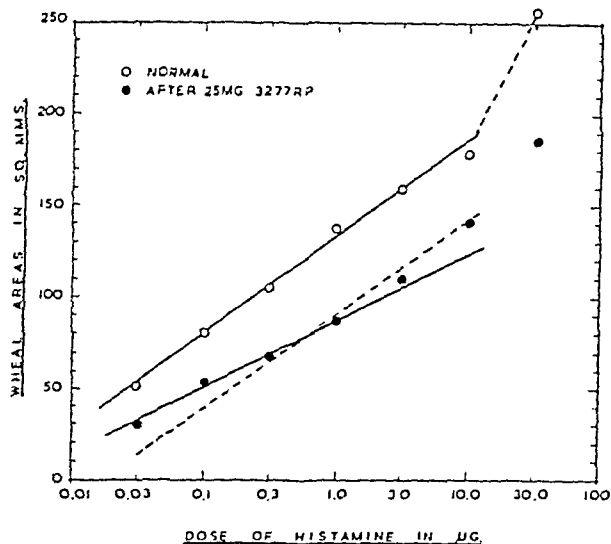


FIG. 1.—To show normal dose-response curve to intradermal histamine and its modification after the oral administration of a histamine antagonist. Mean results from five subjects. Abscissa—dose of histamine base in  $\mu\text{g.}$ , logarithmic scale. Ordinate—wheal areas in sq. mm. The upper (open) points are normal: the lower (solid) ones were obtained three hours after the ingestion of 25 mg. Phenergan (3277 R.P.). For further explanation see text.

The average percentage reduction in wheal area for all the test doses of histamine was 35.0. The lower solid line is drawn to give throughout its course this same percentage reduction of the values represented by the normal dose-response graph. It fits the experimental points more closely than does the broken line which is parallel to the normal graph.

*The comparison of weight-for-weight potencies.*—When a histamine antagonist is taken by mouth the antihistamine effect, as gauged by the percentage reduction in the effect of an intradermal test dose of histamine, rises to a maximum and then tails off, the time relations depending on the conditions of the experiment, the drug used, and the individual. This is illustrated in fig. 2 which shows the mean results with various drugs in the same four subjects. It is clear that, other things being equal, the extent of the maximum reduction of the histamine response will depend on the dose of the antagonist, so that in comparing the relative potencies of different drugs it is essential to make the comparisons when the action of each drug is at its maximum, i.e. when the dose-response curve to intradermal histamine is maximally shifted.

If then, in any subject, the maximum shift of the dose-response curve to intradermal histamine is determined for each of several doses of an antagonist, and this maximum shift for each dose of the antagonist is expressed as the mean percentage reduction in wheal area and plotted as ordinate against log-dose antagonist as abscissa, then the relationship between dose and effect for that antagonist in that subject is determined. By making such observations in a group of subjects a mean dose-response curve for that antagonist is determined. By repeating such observations with other antihistaminics in the same group of subjects mean dose-response curves for these other drugs are obtained, and from such data, since the dose-response curves for the various drugs are parallel, the mean relative weight-for-weight potencies can be readily estimated.

Fig. 3 shows the results of such a comparison of Phenergan (3277 R.P.), Anthisan (Neoantergan, 2786 R.P.) and Antistin.

In these experiments the same six subjects were given, on different occasions, oral doses of 50, 100 and 300 mg. Anthisan, 25, 50 and 100 mg. Phenergan and 100, 200 and 300 mg. Antistin respectively, and the maximum reduction of wheal area was determined for each dose of each drug by at least three intradermal test doses of histamine (10.0, 1.0 and 0.1  $\mu\text{g.}$ ) given before and at intervals after ingestion of the antihistamine.

The areas of the wheals were obtained by inking the wheal outline on the skin five to ten minutes



of Phenergan takes about three and three-quarter times as long to be reduced by half as does the maximum effect of an approximately equi-potent dose of Anthisan, or that the maximum effect of a single dose of Anthisan is reduced by half in about a quarter of the time required for the same degree of reduction after an equi-potent dose of Phenergan. Similarly, the M.D.Q. of Antistin is 5.6.

The remarkable similarity between the half-action times for Phenergan and Anthisan when administered orally, and the corresponding ones obtained when the drugs are infiltrated locally

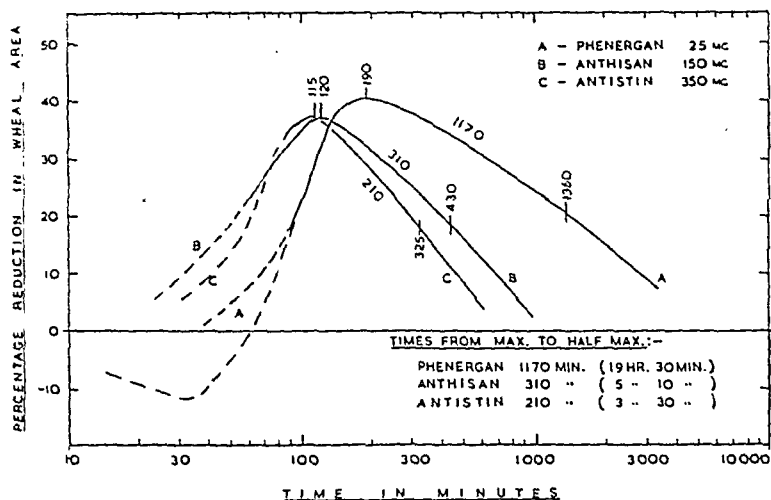


FIG. 4.—To show mean time relationships between onset and disappearance of antihistamine effect with approximately equi-effective doses of different antihistamines administered orally. Mean results from three experiments, each on four or more subjects, with each drug. Abscissa—time in minutes on logarithmic scale. Ordinate—mean percentage reduction in wheal area. Curves A, B, and C are for Phenergan, Anthisan and Antistin respectively. Times to maximum and to half maximum action are indicated for each drug. For further explanation see text.

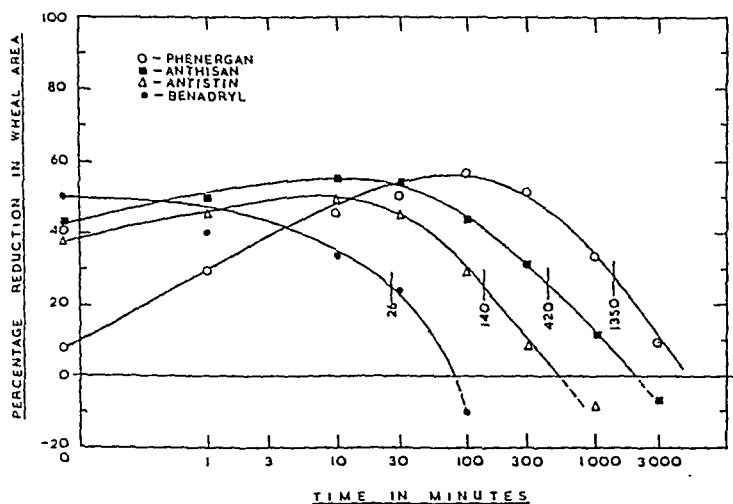


FIG. 5.—To show mean time relationships between onset and disappearance of antihistamine effect when the antihistamine drugs are administered locally to the skin and the test doses of histamine are injected to these infiltrated areas. Results from 14 subjects. Dose of antihistamine—0.2 ml. of 0.1% w/v. Test dose of histamine—1.5  $\mu$ g. base in 0.05 ml. Injections at zero time—i.e. of histamine and the antagonist simultaneously, were of 0.2 ml. containing 0.1% w/v of antihistamine and 1.5  $\mu$ g. histamine base. Indicated on graphs are the times from administration to half-action of the various drugs. For further explanation see text.

of Antistin, is required to produce the effect of a given dose of Phenergan. We can express these differences by saying that, in relation to the maximum effect produced by a single dose, Phenergan is seven times more active, weight for weight, than Anthisan, and fifteen times more active than Antistin. Phenergan, indeed, is by far the most powerful drug of this class which we have encountered and is thus a suitable standard with which the potencies of others can be compared.

Since this method of determining and comparing equi-potent doses of histamine antagonists is of general applicability it is convenient to express the relative potencies of Phenergan and any other antihistamine in terms of what we propose to call the "Mean Potency Quotient" (M.P.Q.), and to define this as the quotient obtained when, for any particular antagonist, the mean dose required to produce a given effect at the time of maximum action is divided by the mean dose of Phenergan required to produce the same effect. The M.P.Q. of Anthisan is thus approximately seven, signifying that, as far as the maximum antihistamine effect of single doses upon the skin capillaries is concerned, seven times as much Anthisan is required to produce the same effect as a given dose of Phenergan, or that Anthisan is weight for weight one-seventh as potent as Phenergan, or that Phenergan is weight for weight seven times more potent than Anthisan. Similarly, the M.P.Q. of Antistin is fifteen. It should be noted that this method of expressing relative potencies states how much more potent Phenergan is than the drug with which it is compared. This convention is adopted in order to avoid fractional quotients. The reciprocal of the M.P.Q. expresses, of course, the potency of any drug as a fraction of the potency of Phenergan.

*Comparison of durations of action.*—From a practical point of view differences in potency among histamine antagonists are probably of less importance than differences in the durations of action; for it is on this latter property that the frequency of administration will depend, and this is an important matter in a class of drugs the use of which is so often associated with unpleasant or disconcerting side-effects and where such effects are usually most evident for a period following the absorption of each successive dose. Fig. 2 gives some idea of the marked differences in the duration of action of some of these drugs; but our problem was to obtain a measure of the relative durations of action such that the differences could be expressed in a fashion analogous to that which we have used for expressing differences in potency. It is evidently impossible to estimate the relative times for the disappearance of the action and so our comparisons have been made by estimating the times taken for the maximum antihistamine effect of single approximately equi-effective doses of the different drugs to be reduced by 50%.

The experiments were carried out on groups of from 4 to 11 subjects. The normal response to intradermal histamine was determined by at least three injections of 1.0 or of 3.0  $\mu$ g. histamine. The drug was then taken with a cup of coffee two or more hours after a light breakfast. The onset and disappearance of the antihistamine effect was determined by duplicate injections of the test dose of histamine at suitable intervals. It was thus possible to estimate graphically for each subject both the degree of maximum effect and the time for establishment of this, together with the time for its reduction by half. The graphs in fig. 2, already referred to, were obtained in this way. They are the average results in four subjects and represent a single experiment. Fig. 4 shows the mean results from three such experiments for the drugs Phenergan, Anthisan and Antistin respectively. In this the times to maximum and to half maximum action are indicated on the graph for each drug.

There is, of course, great individual variation among the results, but the mean values from different experiments are remarkably consistent. Thus while the mean times from ingestion to half action are about 1,360 minutes for Phenergan (1,375, 1,320 and 1,375 minutes) and about 430 minutes for Anthisan (400, 510, 390 minutes) the range among individual subjects is from 700 to 1,800 minutes for Phenergan and 250 to 1,000 minutes for Anthisan.

It will be seen from fig. 4 that Anthisan and Antistin reach full action in about two hours and Phenergan in just over three, and that the mean times from full to half action in these experiments are thus 1,170 minutes (19 hr. 30 min.) for Phenergan, 310 minutes (5 hr. 10 min.) for Anthisan and 210 minutes (3 hr. 30 min.) for Antistin.

As this method of determining and comparing the half-action times after oral administration is applicable to any histamine antagonist, and as Phenergan is by far the longest acting of the drugs we have studied, it is convenient to express the relationship between the half-action time for Phenergan and that for any other antagonist by what might properly be called the "Mean Half-action Quotient", but which we propose to call the "Mean Duration Quotient", or M.D.Q., which we define as the quotient obtained when the half-action time for Phenergan is divided by the half-action time for the drug with which it is compared. This relates the half-action time of any particular antagonist and Phenergan by expressing the half-action time of Phenergan as a multiple of the half-action time of the drug with which it is compared. This convention avoids fractional quotients.

Thus the M.D.Q. of Anthisan is 3.8, signifying that the maximum effect of a single dose

preferred Anthisan; the high preference for Phenergan was clearly based on the relative absence of side-actions with this drug. Thus with Phenergan in nightly doses the appreciated incidence of side-effects, and the severity of these when they occur, is much less than with equi-therapeutic doses of Anthisan given, as it usually has to be, several times a day: hence it should be possible to obtain adequate therapeutic effects by easily tolerated nightly doses of Phenergan in patients unable to tolerate the necessary divided doses of Anthisan.

A diagrammatic representation of the type of data obtained from some of the patients is given in fig. 6. In this case it is evident that the effect of 50 mg. Phenergan lies between that for 600 and for 900 mg. per day of Anthisan. In making the quantitative therapeutic comparison, however, 10 cases have had to be excluded; 8 because the dose of Phenergan used produced a greater therapeutic effect than did the Anthisan in the earlier period of treatment; and 2 because in them the urticaria was not abolished. In the remaining 10 cases the therapeutic effect of a given dose of Phenergan was produced by a total daily dose of Anthisan from eight to eighteen times greater: the average figure was fourteen. Thus, on the average, 25 mg. Phenergan per day is the approximate therapeutic equivalent of 350 mg. Anthisan per day, or of three divided doses each of about 115 mg. Similarly, a nightly dose of 50 mg. Phenergan is the equivalent of about 700 mg. Anthisan per day, or of three divided doses each of about 230 mg.

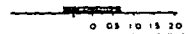
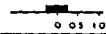
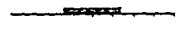






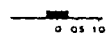


| DRUG      | DOSE<br>(MGS PER<br>24 HR.) | SIDE<br>EFFECTS | INTRACUTANEOUS<br>HISTAMINE REACTION<br>(CM)                                      | URTICARIA | DERMOGRAPHIC REACTION<br>(CM)                                                     |
|-----------|-----------------------------|-----------------|-----------------------------------------------------------------------------------|-----------|-----------------------------------------------------------------------------------|
| NIL       | —                           | —               |  | +++       |  |
| ANTHISAN  | 100<br>100<br>100           | NIL             |  | +++       |  |
| ANTHISAN  | 200<br>200<br>200           | ++              |  | +         |  |
| ANTHISAN  | 300<br>300<br>300           | +++             |  | NIL       |  |
| NIL       | —                           | —               |  | +++       |  |
| PHENERGAN | 50                          | NIL             |  | NIL       |  |

FIG. 6.—To show the type of result obtainable in the clinical comparison of histamine antagonists. Subject W. H., male, aged 23, urticaria present for two years, associated with dermographism. Urticaria: +, occasional wheal; ++, a few wheals; +++, moderate number of wheals. Side-effects: +, slight symptoms on questioning; ++, complaint of mild symptoms; +++, complaint of moderate symptoms. Mean diameter of wheals (thick lines) and flares (thin lines) in cm. Histamine reaction from 0.05 ml. of 0.01% w/v histamine acid phosphate. Dermographic reaction from various traumatizing stimuli (mean of 4 measurements). In this subject 50 mg. Phenergan per day had an effect between that of 600 and that of 900 mg. of Anthisan per day.

With such a relationship between these dose values it is perhaps justifiable to express the relative therapeutic potencies of Phenergan and Anthisan—and, when the information is available, of Phenergan and any other histamine antagonist—in terms of the average ratio between the equi-effective twenty-four hour doses. This "therapeutic ratio" cannot be so called because of the varied connotations which already attach to the expression, and we propose the clumsier "Mean Therapeutic Quotient" or M.T.Q. This can be regarded as stating in respect of the total dose in twenty-four hours, (1) how much more powerful Phenergan is than the drug with which it is compared, or (2) by how much, on the average, a given dose of Phenergan must be multiplied to find the daily dose of the other drug likely to produce the same therapeutic effect as the Phenergan.

The M.T.Q. of Anthisan is about 14. Thus while Phenergan is only about seven times more potent than Anthisan when compared in terms of the single doses required to produce the same intensity of effect (M.P.Q.), it is almost fourteen times more potent than Anthisan when compared in terms of the relative doses per day required to maintain a similar level of antihistamine activity (M.T.Q.). It is clearly the difference in the duration of action of the two drugs, expressed as the Mean Duration Quotient, which is the main factor determining the difference between the mean potency and mean therapeutic quotients.

*Concluding remarks.*—The differences so far noted among the various drugs are differences of degree. But in our first experiment on the duration of action of Phenergan (illustrated in fig. 2) the initial effect of the drug was to potentiate the intradermal histamine response in all four subjects. In subsequent experiments this phenomenon was seen only in some subjects, and the mean curve did not fall below the zero abscissa. These different results are indicated in fig. 4, where alternative routes for the onset of the antihistamine effect of Phenergan are indicated by broken lines. (No other histamine antagonist has exhibited this effect, with the

to the skin, in the manner briefly described in a previous paper (Bain, Hellier and Warin, 1948) and extended and reported on in more detail by Achari *et al.* (1948), is worthy of note. The results of these experiments are shown in fig. 5. It will be seen that the mean times for maximum action to be reached in these circumstances were about 100 minutes for Phenergan and 10 minutes for Anthisan, while the mean times from maximum to half-action were 1,250 minutes (20 hr. 50 min.) for Phenergan and 410 minutes (6 hr. 50 min.) for Anthisan. In view of the similarity of the figures derived from these two different types of experiment it is difficult to escape the conclusion that both the absolute and the relative durations of action of these two drugs are dependent mainly upon their duration of fixation by the tissues on which they act rather than upon, for example, differences in their rates of excretion. Some antihistaminics, however, give markedly discrepant results in the two types of experiment, indicating that such a view is not generally applicable to this class of drugs. Thus some may show a moderate half-action time when administered by mouth, and only a very short half-action time when administered locally. The most striking example is Benadryl, which has an oral half-action time somewhere between that for Antistin and that for Anthisan, but which, on local application (*see* fig. 5), has a half-action time of under 30 minutes. In such instances, where the drugs are not firmly fixed by the tissues, their duration of action must presumably depend mainly on their duration of sojourn in an active form in the extracellular fluid and thus ultimately on their rate of inactivation, or of excretion, or both.

The foregoing comparisons show clearly that histamine antagonists differ markedly in their relative potencies and durations of action. Thus Phenergan is about seven times more potent than Anthisan and about fifteen times more potent than Antistin: the time from full to half-action for Phenergan is about three and three-quarter times greater than that for Anthisan and over five and a half times greater than for Antistin. It is evident that both these factors must be taken into account in assessing the relative merits of both existing and proposed new histamine antagonists.

A further important factor is, of course, the relationship of side-effects to antihistamine activity, for it is the side-effects which at present constitute one of the chief limiting factors in the usefulness of these drugs. We have discussed elsewhere (Bain, Hellier and Warin, 1948; Bain, Broadbent and Warin, 1949) the difficulties associated with the assessment of the incidence and severity of side-effects, and have stated earlier in this paper that we have not dealt with these in a quantitative fashion. We hope, however, that it may be possible to devise a semi-quantitative treatment of side-effects by applying to them a system of "scoring". The "scores" obtained in the same group of subjects by different drugs could then be used to derive a "Mean Side-Effect" or "Mean Toxicity Quotient". Determined on equi-potent doses of different drugs this might indicate the relationship, if any, between the most interesting side-actions—those which are so similar to the effects of hyoscine—and the specific antihistamine effect itself. But from the clinical point of view it would also be important to compare equi-therapeutic as distinct from equi-potent doses and this would clearly give a different quotient, the difference depending to a large extent on the relative durations of action of the drugs compared. This will be evident from the observations about to be described.

*Comparison of therapeutic potencies.*—We have so far been able to make a therapeutic comparison of only two drugs—Phenergan and Anthisan. As details of this comparison are presented elsewhere (Bain, Broadbent and Warin, 1949) only a summary will be given here.

In 20 patients with chronic urticaria the reaction to intradermal test doses of histamine and, when present, the dermatographic reactions to various stimuli, were measured by Dr. Warin before and at intervals after the institution of therapy with Anthisan, and compared with the progress of the urticaria. The Anthisan was given two, three, or four times a day, as was found necessary. After a rest period the control observations were repeated and the patients put on Phenergan. In view of the long duration of action of this drug it was given in a single dose at night. Given in this way we hoped that the drowsiness which it often causes would not contribute to sleep and that any other side-actions would pass unnoticed, whereas the antihistamine effect would continue throughout the following day. An attempt was made to adjust the dose of Phenergan so as to give the same therapeutic effect as with Anthisan in the earlier period of treatment: we hoped to be able in this way to establish the approximately equivalent therapeutic doses.

While Anthisan had usually to be given three or four times a day the nightly dose of Phenergan controlled the urticaria in all the patients throughout twenty-four hours. Only 3 patients were completely free from side-effects with Anthisan against fourteen on the nightly dose of Phenergan. The only side-effect noticed with Phenergan was morning drowsiness, but in only 5 patients did this persist throughout treatment. 14 patients preferred Phenergan, 5 had no preference and only one

by antagonizing the action of histamine on the capillaries, by a receptor competition mechanism, on the one hand, and by diminishing the release of histamine from the tissues, by some unknown mechanism, on the other. We have evidence, indeed, from other lines of work that histamine antagonists may in certain circumstances act in this latter fashion. But much further work is needed before any discussion of the various possibilities concerning the mode of action of histamine antagonists can be justified on the basis of experimental work on man; the view just expressed is therefore to be regarded as little more than a speculation.

#### SUMMARY

(1) Methods of comparing the weight-for-weight potencies, relative durations of action, and relative therapeutic efficacies of histamine antagonists are described, but statistical treatment of the data is omitted.

(2) The outstanding potency and duration of action of Phenergan (3277 R.P.) suggests its suitability as a standard against which these properties of the others can be compared.

(3) Relative weight-for-weight potencies are expressed in terms of the "Mean Potency Quotient" obtained by dividing the mean dose of the drug under test which produces a given mean antihistamine effect, by the mean dose of Phenergan which produces the same effect. The quotient states how much more powerful Phenergan is than the drug with which it is compared, or by how much the dose of the drug under test must be multiplied to give the same effect as a given dose of Phenergan. The M.P.Q. of Anthisan is about 7 and of Antistin about 15.

(4) Relative durations of action are expressed in terms of the "Mean Duration Quotient", obtained by dividing the time from maximum to half-maximum action for Phenergan by the corresponding time for an approximately equi-effective dose of the drug under test. This expresses the half-action time for Phenergan as a multiple of the half-action time of the drug with which it is compared. The M.D.Q. of Anthisan is 3.8 and of Antistin 5.6.

(5) Relative therapeutic efficacies in chronic urticaria may be expressed in terms of the "Mean Therapeutic Quotient", obtained by dividing the daily dose of the drug under test by the daily dose of Phenergan required to produce an equal therapeutic response. This expresses the therapeutic potency of Phenergan as a multiple of the potency of the drug with which it is compared, or states by how much the daily dose of Phenergan must be multiplied to give the equivalent daily dose of the other drug. The M.T.Q. of Anthisan in chronic urticaria is about 14.

(6) A possible qualitative difference between Phenergan and the other drugs is noted, and some aspects of the probable mode of action of histamine antagonists are briefly discussed.

The cost of this work was met by a grant from the Medical Research Council.

#### REFERENCES

- ACHARI, G., BAIN, W. A., BROADBENT, J. L., and ROBINSON, M. (1948) Communication to British Pharmacological Society, July.  
 BAIN, W. A., BROADBENT, J. L., ROBINSON, M., and WARIN, R. P. (1948) Communications to British Pharmacological Society, July.  
 —, —, and WARIN, R. P. (1949) *Lancet* (ii), 47.  
 —, HELLIER, F. F., and WARIN, R. P. (1948) *Lancet* (ii), 964.  
 DALE, H. H. (1948) *Brit. med. J.* (ii), 281.  
 GADDUM, J. H. (1948) *Brit. med. J.* (i) 867.  
 HALPERN, B. N. (1948) in *Acquisitions Médicales Récentes*. Flammarion, Paris, p. 251.  
 HUNTER, R. B., and DUNLOP, D. M. (1948) *Quart. J. Med.*, 17, 271.  
 KAPPELLER-ADLER, R. (1949) *Biochem. J.*, 44, 70.

**Dr. H. O. Schild:** *The Experimental Evidence for the use of Antihistamine Drugs in Allergic Conditions.*

The following experimental facts form the basis for the use of antihistamine drugs in allergic disease:

- (1) Histamine is released in anaphylaxis.
- (2) Antihistamine drugs abolish the actions of histamine on plain muscle.
- (3) Antihistamine drugs diminish or abolish the anaphylactic reaction in the whole animal and in isolated sensitized plain muscle.

When these drugs are used in allergic conditions in man, however, certain inconsistencies appear which are difficult to explain at first sight. For instance, antihistamine drugs are almost inactive in bronchial asthma, and are most active in capillary conditions such as urticaria and hay fever (Hunter and Dunlop, 1948). When, however, histamine is injected into the blood-stream its bronchoconstrictor effects are readily abolished by antihistamine drugs, more readily indeed than its vasodilator effects.

Dale (1948) distinguishes between the actions of intrinsic histamine and those of extrinsic histamine. The former are actions produced by histamine on the tissues from which it is released; the latter are actions on tissues to which histamine is carried after release. Obviously antagonism by an antihistamine drug may be very different in the two cases. The actions of extrinsic histamine might be expected to correspond closely to those of injected histamine. It can be shown, in fact, that the action of histamine released from tissues

possible exception of Antistin: but with this the only evidence was indirect—the somewhat late rise of the curve (see fig. 2) from the zero line.) A similar potentiation of the intradermal histamine response has often been noticed—but again only in some subjects—when Phenergan and histamine have been injected to the skin in experiments of the kind illustrated in fig. 5. The effect was most commonly seen when the two drugs were administered simultaneously.

We sought to account for this phenomenon by the hypothesis that Phenergan might antagonize histaminase. Some support is perhaps given to this view by the work of Kapeller-Adler (1949) who has shown that Phenergan and Antistin inhibit the action of histaminase *in vitro*, but that none of the other histamine antagonists investigated do so.

If the primary potentiation of the intradermal histamine response with Phenergan is due to partial inhibition of histaminase then it is clear that the fixation of the drug by the enzyme occurs very quickly, in marked contrast to the rate of fixation by the capillaries. But to what total extent histaminase may be inactivated by therapeutic doses of Phenergan, or how long the effect may persist, it is impossible from our experiments to say, because the effect itself, manifested by the potentiation of the wheal response, becomes quickly masked by the establishment of the specific antihistamine action of the drug. However, if Phenergan is potent as an inhibitor of histaminase it is possible that therapeutic doses of the drug in persons relatively resistant to the antihistamine effects might produce an exacerbation of any symptoms due to histamine release; such untoward effects could presumably be countered by increasing the dose.

It is generally assumed that histamine antagonists act by receptor competition—that they become fixed, in varying degree and with varying firmness, to receptors on the tissues on which histamine acts, and, by this preferential fixation or competition, partially exclude or block the access of histamine to these receptors (Gaddum, 1948). The failure of histamine antagonists to diminish histamine-induced gastric secretion may be due to a difference in the histamine receptors in the gastric glands such that the antagonists fail to become fixed to them. Of the actions of histamine which are influenced by histamine antagonists those due to injected (exogenous) histamine are usually held to be more readily affected than those due to histamine released by the tissues (endogenous histamine). Furthermore, Dale (1948) distinguishes between histamine which is released by the cell on which it reacts and that which when released acts only upon more remote structures: the former he calls intrinsic and the latter extrinsic histamine. In man the antihistamine drugs are usually much less effective against intrinsic than against extrinsic actions of endogenous histamine. They are—assuming the role of histamine in these conditions—less effective, for example, in bronchial asthma, where the histamine is liberated by the reacting structure, than in chronic urticaria where it is not. But it may be that the relative failure of histamine antagonists to block intrinsic actions is due simply to the difficulty, with the agents at present available, of reaching an effective drug level at the site of histamine release with doses of the drugs which are tolerable. In chronic urticaria, on the other hand, the histamine does not act upon the cells from which it is liberated but upon the capillaries with which it subsequently comes in contact through humoral channels. Histamine antagonists are thus regarded as effective in urticaria because the liberated histamine acts in a fashion analogous to that of histamine injected from outside.

Nevertheless it may be wondered how antihistamine drugs can abolish urticaria when, according to the pharmacological data summarized earlier in this paper, very large doses may be required to produce a 70% reduction in the intradermal histamine wheal response and quite intolerable doses are theoretically required to abolish it. Nor is it only when histamine antagonists are administered orally that we have failed to abolish the intradermal histamine response, for we have failed equally to do so when the drugs are administered locally to the skin. The average maximum percentage reduction obtained by local administration, even of Phenergan, was about 60% (see fig. 5) and the maximum individual reductions seldom exceeded 80%.

Chronic urticaria is in fact abolished, however, when the area of the intradermal wheal response is reduced by, on the average, about 50% with a range of individual values from 30% to about 80%. On the other hand, the average percentage reduction in the dermographic wheal response at the stage when urticaria is cleared is of the order of 90% (range 86–96%). This type of difference is illustrated in fig. 6 where, with the 50 mg. dose of Phenergan, the dermographic wheal response is reduced by about 90% and the intradermal histamine wheal response by 70%. Unfortunately we have but few observations of this kind on the dermographic response. Nevertheless if this sort of result can be confirmed and the quantitative differences between the effects of the drugs on injected and on liberated histamine respectively can be shown not to be due to the different circumstances attending the production of the two types of reaction, then it will be difficult to escape the conclusion that, in the relief of chronic urticaria the histamine antagonists may be exhibiting a dual modality of action—

In some cases the beneficial effects of antihistamine drugs may not be due at all to antagonism to histamine, but to some independent pharmacological action. Antihistamine drugs, like all antagonistic drugs, are not entirely specific. In low concentrations they antagonize only histamine, but in higher concentrations they antagonize the actions of acetylcholine (Schild, 1947) and presumably of other stimulant agents. Although none is completely specific, some antihistamine drugs are more specific than others. Reuse (1948) has shown that 3277 R.P. (Phenergan) besides being a very powerful antagonist of histamine also strongly antagonizes acetylcholine. Benadryl, though weaker, also possesses both actions. By contrast Neoantergan (Antihistone) is a very strong antagonist of histamine but only a weak antagonist of acetylcholine. Halpern (1948) has shown that antihistamine drugs affect capillary permeability. They counteract increases in capillary permeability produced not only by histamine but also by other capillary dilators. 3277 R.P. (Phenergan) is particularly active in this respect.

To summarize: We now possess drugs with extremely powerful antihistamine action (except on gastric secretion) and in some cases with remarkable activity against the anaphylactic response. It is probable, however, that the two actions do not run strictly parallel. Furthermore, it is doubtful whether the anaphylactic reaction in animals can be wholly equated with human allergic reactions. It follows that antihistamine drugs, like all drugs, cannot be completely assessed by animal work. The preliminary work must of necessity be done in the laboratory, but the eventual appraisal of each individual drug can only be made by assessing it in patients exhibiting the disturbance against which the drug is to be used.

#### REFERENCES

- BARSOUM, G. S., and GADDUM, J. H. (1935) *J. Physiol.*, **85**, 1.  
 DALE, H. H. (1948) *Brit. med. J.* (ii), 281.  
 HALPERN, B. N. (1948) in *Acquisitions Médicales Récentes*. Flammarion, Paris. p. 251.  
 HUNTER, R. B., and DUNLOP, D. M. (1948) *Quart. J. Med.*, **17**, 271.  
 LOEW, E. R. (1947) *Physiol. Rev.*, **27**, 542.  
 REUSE, J. J. (1948) *Brit. J. Pharmacol.*, **3**, 174.  
 SCHILD, H. O. (1936a) *Quart. J. exp. Physiol.*, **26**, 165.  
 — (1936b) *J. Physiol.*, **86**, 51P.  
 — (1939) *J. Physiol.*, **95**, 393.  
 — (1947) *Brit. J. Pharmacol.*, **2**, 189.  
 — (1949) Unpublished results.

#### Dr. Ranyard West (Edinburgh): *Bronchospasm and Antihistamine Drugs.*

The antihistamine drugs have been so named because, under certain conditions of administration, they antagonize many observed actions of histamine. The conditions of successful administration of these drugs are not always easy to determine; and certain actions of histamine, notably that of gastric secretion, remain unopposed by all existing "antihistamine" drugs. It is therefore impossible to say of a histamine-like effect: "Because this action is not antagonized by Neoantergan or Benadryl or Antistin, therefore it is not due to histamine".

When the fame of the antihistamine drugs was experimentally established and they came to be considered as safe therapeutic agents, there was naturally enough a rush to exhibit them in asthma, since in some animals bronchospasm is an observed action of histamine and it had frequently been suggested (though it was as frequently denied) that the bronchospasm of asthma might sometimes be due to the liberation of histamine or a histamine-like substance in the bronchial tree of asthmatics. On the whole we may say that the results of such treatments, although not entirely negative in the hands of some workers (Waldbott, 1947; Herxheimer, 1948) were disappointing (Hunter and Dunlop, 1948). Up to date it cannot be said that antihistamine drugs abolish or prevent the bronchospasm of asthma, under well-controlled conditions of administration, with any constancy or even with results which suggest that success is just round the corner. That fact has created a disappointing situation in the field of therapy.

But apart from clinical asthma there is another condition of bronchospasm in which histamine-liberation has been invoked as the effective bronchoconstrictor agent. I refer to curare-bronchospasm. Curare-bronchospasm was first described in 1935 as an irregularly occurring complicating action of crude curares. The action appeared to vary from one specimen of curare to another and to show a species variation, being particularly marked in rodents and not uncommon in dogs, while it was more rarely found (though it could occur) in the cat (West, 1935). At that time our chemical collaborators, Dr. Harold King and Mr. A. Stephens, were constantly providing us with new, impure alkaloidal fractions from crude curares, and plant material from British Guiana was yielding increasingly pure chemical material for pharmacological trial. Some of these fractions possessed a greater power of causing bronchoconstriction than did others; and at one time we were inclined to think

corresponds in every respect to that of synthetic histamine, and that both are equally antagonized by antihistamine drugs.

Many inconsistencies would be explained if it could be assumed that in those instances where the antihistamine drugs are most effective extrinsic histamine is concerned. For instance, in hay fever histamine might be released from epithelial cells and thence diffuse to the blood-vessels. In this way its action on blood-vessels might be easily antagonized. Unfortunately we lack direct evidence that histamine is released from tissues in human allergy, as is the case in experimental anaphylaxis. The problem is essentially technical owing to the difficulty of demonstrating the presence of minute amounts of histamine in plasma and tissue fluids. Positive results might possibly be achieved by using techniques based on diffusion of histamine from sensitized tissues into Ringer's solution containing the antigen (Schild, 1939). These techniques might be applied to slices of tissue removed during operations from patients exhibiting some specific allergy.

The effects of antihistamine drugs on intrinsic histamine are more difficult to appraise. When histamine is released in anaphylaxis the total quantity released can be measured, but the effective concentration at the cell membrane at the time of release is unknown. It is therefore impossible to estimate how much antihistamine is required to antagonize these actions.

In general the anaphylactic reaction of plain muscle is more difficult to suppress than the reaction to extrinsic histamine (Loew, 1947). For instance, equal concentrations of antagonist are needed to antagonize the actions of 500  $\mu\text{g./ml.}$  extrinsic histamine and of 5  $\mu\text{g./gramme}$  intrinsic histamine on bronchial muscle (Schild, 1936a). This might be due to a hundredfold concentration of intrinsic histamine at the cell membrane, but other experiments indicate a qualitative as well as a quantitative difference. For instance, the isolated uterus of a sensitized guinea-pig can be made completely irresponsive to extrinsic histamine and yet continue to respond to the specific antigen (Schild, 1936b).

This experiment is illustrated in fig. 1. In this case the antihistamine drug used is histamine itself, in some ways the most specific antagonist of histamine (Barsoum and Gaddum, 1935), since when present in excess it presumably blocks all the "receptors" for histamine. Why is it that the muscle still continues to respond to the specific antigen? Granted that histamine is released from the uterus during the anaphylactic reaction (Schild, 1939), how does intrinsic histamine reach the receptors which are already blocked? Is it that intrinsic histamine reaches certain intracellular receptors which cannot be reached by histamine added from outside? This explanation is rendered less likely by the finding that histamine added from outside diffuses readily into the cell interior (Schild, 1949). Whatever the explanation of the experiment shown in fig. 1, its significance lies in the fact that it shows that in principle anti-anaphylactic and antihistamine actions can be separated.

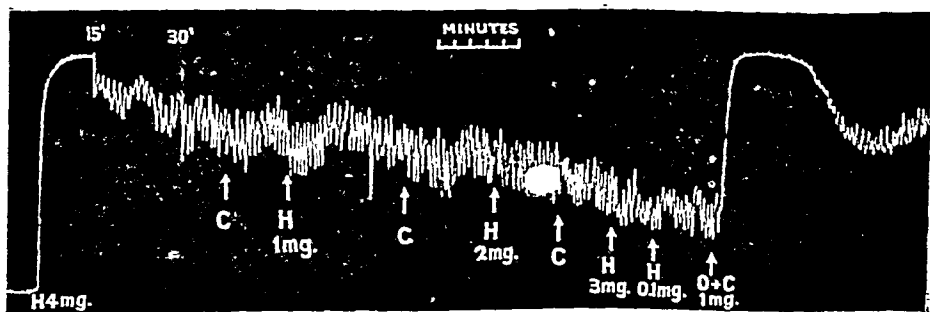


FIG. 1.—Contractions of the isolated uterus of a guinea-pig which had been previously sensitized to egg albumen. Uterus suspended in 20 c.c. bath in Ringer's solution. Addition of histamine to the bath at first produces contraction, but gradually the muscle relaxes in spite of the continued presence of histamine, and shows no more response to further additions of histamine acid phosphate (H), or sodium acid phosphate (C). When, however, the specific antigen, egg albumen (O), is added, it contracts maximally. This experiment shows that it is possible to abolish the response to extrinsic histamine and yet preserve the anaphylactic response of plain muscle.

Antagonists of histamine may thus be expected to relieve readily those pathological conditions in which histamine acts at some site in the body different from the original site of release, but they may be expected to be rather less active, and possibly, in some cases, inactive, at the site of the primary allergic reaction itself.



In a valuable investigation of curare bronchoconstriction in dogs an infant resuscitator has been used by Landmesser (1947). In these experiments the diaphragm was paralysed by spinal anaesthesia in order to obviate the confusing effect of passive bronchoconstriction, the histamine controls were effective, and the author was satisfied that he demonstrated active bronchospasm from the use first of "intocostin" and later of pure *d*-tubocurarine and "curarine chloride". The element of inconstancy of the reaction is emphasized by his results: for though "intocostin" caused bronchoconstriction in five cases out of five, *d*-tubocurarine produced bronchoconstriction only seven times out of ten, and bronchodilatation in two of the remaining three. "Curarine chloride" (impure calabash "curarine"?) was rather more prone to cause bronchospasm than was *d*-tubocurarine. Repeated small doses of the curare preparations had diminishing effects, while a subsequent large dose might cause increased bronchoconstriction. Landmesser made the additional observation that such curare bronchospasm in dogs is both preventable and removable by the antihistamine drugs Pyribenzamine and Benadryl (Landmesser, 1947). More recently Mahfouz (1949) has examined the action of *d*-tubocurarine chloride on the exposed guinea-pig lung, using the air-shunt method. He reported bronchoconstriction as present, not constantly, but in 9 of 16 consecutive cases. He has so far observed no alternative bronchodilatation. The bronchospasm is both removable and preventable by Neoantergan. Mahfouz adds that bronchospasm is much less likely to occur in this preparation if the injection of *d*-tubocurarine is given slowly. After curare bronchospasm has occurred, second doses of *d*-tubocurarine are ineffective, while injected histamine remains as effective as before.

The investigations described in the foregoing paragraph were undertaken because of the introduction (Griffith and Johnson, 1942) and extensive use of curare extracts in anaesthesia in recent years and the occasional reports of fatalities due to alleged bronchial spasm (Whitacre and Fisher, 1945; Holoday, 1946). Though all such cases involve the difficult separation of active bronchospasm—which may itself occur from reflex causes unconnected with the use of curare (de Takats *et al.*, 1942)—from passive collapse of the lung, when curare is employed these two conditions may occur together and reinforce each other. It does now appear reasonably certain, however, that at least one pure alkaloid of curare much used in anaesthesia, namely *d*-tubocurarine chloride, is capable under certain conditions of producing active bronchospasm, though it may do so with less readiness than some other curare derivatives.

With regard to the method of production of curare bronchospasm, we have first of all the evidence that perfusing curare (including calabash "curarine") through voluntary or cardiac muscle will liberate histamine in rapidly diminishing quantities until the muscle store is depleted (Anrep and Barsoum, 1935; Alam *et al.*, 1939), and that this also applies, under certain conditions and at least in certain species, to the tissues of the bronchial tree (Schild, 1948). Though the amounts of histamine recoverable from the perfusates may be small, we do not know the histamine concentration at the actual site of liberation; nor do we know the dose of histamine required for muscle contraction when this substance is released in effective proximity to an appropriately sensitive smooth muscle. Histamine is subject to attack by histaminases just as acetylcholine is by cholinesterase; and as it proved with acetylcholine as an excitator of normal voluntary muscle, so may the endogenous liberation and action of histamine (whether it be in intestine, heart or lung) be of so intimate and transitory a nature as continuously to elude detection until some necessary development and improvement of technique has taken place. By the same token antihistamine drugs must not be confused with histaminases. Their action may be more like that of atropine upon the mediation of muscular contraction by acetylcholine, effective only at certain sites and under certain limited conditions. They are not specific antagonists, and the term "antihistamine" is, in a sense, a misnomer.

Landmesser has concluded that curare probably causes bronchoconstriction where it does so by liberating histamine locally in the muscles of the bronchial tree. The evidence for this is cumulative—the similarity of action, the progressive discovery of histamine in curare perfusates, a diminishing efficacy of action comparable to the diminishing curare-liberation of histamine found (Alam *et al.*, 1939) in dogs, a certain inconsistency of the findings which is characteristic of physiological effects produced by histamine, and antagonism by "antihistamine" drugs. Not one of these pieces of evidence is conclusive; many different drugs have similar actions, the presence of histamine may be incidental, "antihistamine" drugs have other actions, among them an antagonism to acetylcholine. Cumulatively the presumptive evidence that something very like histamine pursues its pharmacological effects upon the bronchi when it has been locally released by an action of curare on muscle may now be considered to be fairly strong. Such a presumption is strengthened and not weakened by the "histamine reactions" of the skin following intracutaneous and intra-arterial injections of *d*-tubocurarine reported by Comroe and Dripps (1946) and their prevention by antihistamines (Grobbs *et al.*, 1947).

that we were merely dealing with an impurity separable from the alkaloids which caused the classical curare action of myoneural paralysis.

It so happened, however, that the only reasonably pure (though never definitely crystalline) alkaloid with which Dr. King was able at that time to supply me in any considerable quantity had both a strong "curarizing" action and also showed this action of variable bronchoconstriction, with species variation towards rodents and dogs but also affecting man. This alkaloid was calabash "curarine". Boehm, 1895, obtained in this case direct from the bark of *Strychnos toxifera*, an accepted ingredient of Guianese curare.

In man curare bronchospasm produced by calabash "curarine" occurred as an occasional sudden severe bronchoconstriction when curarine was given in subparalytic doses to cases of tetanus, spastic paraplegia and post-encephalitic Parkinsonism (West, 1936). It could occur in patients who appeared to be only lightly curarized. Its analysis was undertaken in the hope that curare derivatives would find a useful place as "lissive" agents in removing pathological muscular rigidities in diseases of the nervous system (West, 1932).

In curare "asthma" it is necessary to separate the two elements of active and passive bronchoconstriction. Passive bronchoconstriction is produced by the classical action of curare upon the respiratory muscles, with a resultant fall of intrapleural suction (or "negative pressure") during inspiration. It leads ultimately to a passive collapse of the lungs. Active bronchoconstriction is due to a maintained contraction of the circular muscle of the bronchi in response to a local stimulus. It is impossible to speak with confidence of bronchospasm in connexion with any curarizing drug unless this separation has been made.

Active curare bronchospasm, thus separated from passive components, can be demonstrated in animals as follows: (1) by directly observing the intact exposed lungs in guinea-pigs; (2) by recording minimal distension pressures of the exposed guinea-pig lung; (3) by perfusing an isolated strip of bronchial muscle in a water-bath.

*Method 1.*—By this method, in which the guinea-pig is pithed, the diaphragm incised and ventilation maintained by positive pressure with a pump, calabash "curarine" produced a reduction of lung movement, but never, even with very large doses, did it produce the instant abolition of lung expansion which is characteristic of histamine given by injection. The lungs also became more cyanosed, giving the impression that effective oxygenation ceased at a lesser reduction of lung movement with curarine than with histamine (West, 1938).

*Method 2.*—Apart from such direct observation active bronchospasm can be recorded by measuring the "minimal distension pressures" of the guinea-pig lung, or alternatively the shunt of air to a side tube which is produced when the air-space of the exposed lung is diminished by bronchoconstriction, the record being made either with a water manometer or a tambour. The author used a water manometer recorder and by it found that "curarine" produced a rise of seven to ten times the initial distension pressure by a bronchoconstrictor effect which was abolished by adrenaline. The effect could not be increased by raising the dose of "curarine". Small doses of histamine always produced a greater bronchoconstriction than did curarine. Its effects were also removed by adrenaline; but with histamine increased dosage proportionately increased the severity of the bronchospasm (West, 1938).

*Method 3.*—The reaction of the bronchial muscle can be studied more intimately by adding the drug to a water-bath containing a strip of muscle attached to two or three rings of the trachea suspended from a reflecting mirror recorder. This is a classical pharmacological experiment in which histamine produces an instant bronchospasm. Curarine in high concentrations also produces a severe bronchoconstriction, but only after a delay of about eight minutes, which suggested to us even at that time that some progressive reaction must be under way in the water-bath between the "curarine" and some substance within the muscle fibres of the trachea. As with histamine the spasm is readily and instantly removed by adrenaline (West, 1937).

Among methods of measuring bronchial narrowing which may confuse active bronchospasm with passive bronchoconstriction are those which involve the creation of an artificial pneumothorax. This may be done in two ways. In one of them, useful in the guinea-pig, a pointed metal cannula with perforated sides is thrust through the posterior mediastinum to a point where at least one perforation transmits a freely swinging pressure, or suction, from the pleural cavity to a connected tambour (Jackson, 1917). In larger animals, such as rabbits and cats, a small pneumothorax may be induced, as in man, by a hollow needle thrust between the ribs and attached to a water manometer to record intrapleural pressures (West, 1938). With either method it is necessary to realize that, where the bronchoconstriction of a curarizing agent is under examination, the effect of partial curarization will be recorded as a "fall" of negative intrapleural pressure and thus oppose the recording of any active bronchospasm which "increases" by suction the negative pressures in the closed recording system. By a combination of active bronchospasm and passive bronchoconstriction it is possible for a severe collapse of the lung to occur without a greater change in the intrapleural pressures than may occur with deep ether anaesthesia. Without great care in handling and analysis, therefore, the results of such methods of recording are unsuitable to the estimation of bronchoconstriction produced by curarizing drugs.

## Section of Pædiatrics

President—Professor J. M. SMELLIE, O.B.E., M.D., F.R.C.P.

[February 25, 1949]

### DISCUSSION ON PLANNING A PÆDIATRIC UNIT IN AN UNDERGRADUATE TEACHING HOSPITAL (WITH A TRAINING SCHOOL FOR NURSES). [Abridged]

Dr. A. Doyne Bell, and Mr. A. S. Gray, F.R.I.B.A. : The subject of the architectural planning of a Children's Unit, if discussed in general terms, is a confused one. We intend to confine ourselves to the special conditions imposed by the Pædiatric Unit being part of a General Teaching Hospital.

In planning modern units the criteria laid down by J. Crooks and S. E. T. Cusdin (1947) still hold good : (1) The prevention of infection from patient to patient (and from staff to patient). (2) The constant supervision of sick children. In connexion with this second criterion it is to be noted that a greater number of nurses *per capita* are required in a children's unit than in a unit nursing sick adults.

A third factor which must be given careful consideration is the maximum possible happiness of the sick child while in hospital. The psychological effect of taking children away from their homes during illness has been much discussed lately (Spence, 1947). In these discussions the desirability of allowing parents to take a part in the care of sick children has been canvassed, and the putting into practice of such an idea, combined with a possible relative shortage of skilled nurses in the future, may well lead to modification of design so as to render certain aspects of the technical side of nursing more foolproof.

If it is assumed that the General Teaching Hospital of the future will have approximately a thousand beds, then it seems that a hundred of these beds should be allocated to pædiatrics. Within the Department of a hundred beds provision must be made for :

- (a) Surgical cases.
- (b) Sick infants (some the produce of the obstetric department).
- (c) Infectious cases (either arising in the course of non-infectious disease in in-patients or cases admitted for observation and subsequently diagnosed as infectious).
- (d) The "run of the mill" pædiatric cases.

#### LOCATION OF THE DEPARTMENT

The Pædiatric block would best be placed where the noise of the children crying or at play will not disturb other patients. Its nearness to any special departments not included in the Unit but used frequently by the Unit is desirable.

#### SPECIAL DEPARTMENTS

The next question for consideration is, what special departments shall be duplicated for exclusively pædiatric purposes? Those whose experience has been largely confined to children's hospitals tend to stress the importance of exclusively pædiatric radiological departments and, with less insistence, pædiatric laboratory facilities. Those of us who have had experience in both children's hospitals and general hospitals are less sure that this duplication secures the highest efficiency. It is clear that certain cases will arise in which the experience of a radiologist, trained in the special technique, will be of more value than that of a radiologist better acquainted with children but less well acquainted with such technique.

spirochæte on artificial media has not yet been accomplished in any of the six laboratories in which the problem is under study; but survival for ten to fourteen days has been achieved. This result, hopeful of still further progress, has led to an important immunologic advance, described briefly in the next paragraph.

*Treponemicidal antibody.*—Nelson and Mayer, working at the Johns Hopkins University, have shown that in the serum of syphilitic rabbits or man, but not of normal rabbits or man, or in a limited number of persons suffering from infections or diseases other than syphilis, there is present an antibody which immobilizes and kills virulent *T. pallidum*. By appropriate adsorption experiments, this antibody is shown to be distinct from reagin. This important advance opens new avenues of approach to a study of the biology of syphilitic infection, immunity, and the possible development of a new and specific test for syphilis. It is of probable value in the practical problem of differentiation of true from biologically false positive blood tests.

*Strains of T. pallidum.*—Fresh experimental work has demonstrated immunologic differences, and variations in penicillin-sensitivity, of several different strains of *T. pallidum*.

*The penicillin therapy of syphilis.*—The advent of procaine penicillin has raised the possibility of the cure of early syphilis with a single injection of the drug. Procaine penicillin is a highly insoluble salt. When suspended in oil plus 2% aluminum monostearate, a single intramuscular injection of 0.6–1.2 mega units provides a measurable blood level (0.03 u./c.c.) for five to seven days. When this drug is administered in a single dose of 0.6–0.9 mega units to persons exposed to infectious syphilis, the incidence of development of early syphilis is reduced from about 60% (in a control untreated series) to about 5%. This is a practical application of abortive early treatment, based on the facts that in any infection, penicillin dosage may be reduced in proportion to the age of the infection and the number of infecting organisms.

*Failure rates in early syphilis in relation to serologic pattern.*—An elaborate clinical and serologic study has shown that in early syphilis, clinical outcome measured in terms of early relapse, within the first three to four years, is closely related to type of serologic response.

*Prenatal syphilis.*—Further experience confirms the fact that penicillin is far superior to any other method of treatment in the prevention of prenatal syphilis, the failure rate in terms of syphilitic infants remaining at 1 to 2%. It has also been shown that if "adequate" metal chemotherapy or penicillin has been administered to a syphilitic woman, re-treatment during every subsequent pregnancy is not necessary. These facts are of major public health importance.

*The Jarisch-Herxheimer reaction.*—In both early and late (especially neurosyphilis) infections, the febrile response following the initial dose of penicillin is an all-or-none phenomenon, which does not occur with doses of 10 u./kg. or less; but does occur with equal frequency and severity with a larger dose of any amount. From the practical point of view, the reaction cannot be avoided by the initiation of treatment with small doses. Clinically, the reaction is not troublesome except in general paralysis of the insane, where it may be serious.

The remainder of the paper is devoted to a discussion of (a) the dynamics of penicillin action and (b) newer antibiotics in the treatment of the venereal diseases, sections which do not readily lend themselves to abstraction.

Bibliographic documentation is provided in the original article.

the ward of twenty beds to which they are attached. In addition we have planned the following departments to be shared between two wards of twenty beds:

- (a) A teaching room.
- (b) A fluoroscopy screening room.
- (c) A consulting room.
- (d) A nurses' cloakroom.
- (e) Ward offices (social workers, notes, &c.).
- (f) Visitors' night room.
- (g) Admission bathroom.
- (h) Visitors' waiting-room (day).

It is felt that these rooms could be shared by two units without friction. The visitors' night room might well be fitted with bunks. These could give the standard of comfort of a first-class railway sleeping-car and, at the same time, be economical of space and convey to the mind of the visitor that they are intended as purely temporary accommodation.

The teaching room would be used for conferences and for clinical students writing their notes.

*Nursing mothers.*—It is a matter for discussion whether the nursing mothers of sick babies should be accommodated in the Unit or in a special mothercraft department elsewhere in the hospital. In our plan we have provided two separate rooms in the common wing of the two units which might be used for this purpose. A special mothercraft department would, however, serve the double purpose of housing the healthy nursing mothers of sick infants and the healthy suckling infants of sick mothers. It would be an excellent training school for nursery nurses and a source of instruction in breast feeding to the obstetric and paediatric students.

*Infectious block.*—A unit of twenty beds in which all the beds are in single cubicles is planned in the treatment of infectious diseases. There will of course be no day-room needed in this unit.

#### REFERENCES

- CROOKS, J.; and CUSDIN, S. E. T. (1947) *Arch. Dis. Child.*, 22, 106.  
 SPENCE, J. C. (1947) *Brit. med. J.* (i), 125.  
 WATKINS, A. G., *et al.* (1946) *Brit. med. J.* (i), 673.

#### THE DISCUSSION

The consensus of opinion, led by the Chairman, seemed to be that a Children's Unit should have a special radiology department, as an independent section within the main radiological department of the hospital. The volume of work in an adult unit was considerably less than that in a Children's Unit.

It was agreed that sisters should not be asked to share kitchens.

The prevention of cross-infections in a gastro-enteritis unit was stressed. Destructible napkins should be used and incinerated. The problem of the disposal of soiled linen in this unit was discussed and it was agreed that special facilities would be needed. The soiled linen should not come into the corridor of the unit.

The undesirable effect on the students of separating the Paediatric Unit from the teaching hospital was a matter of agreement. Paediatrics was better able to take its proper place in the general training of the student if the Unit were contained within the general teaching hospital. The advantages to the staff of daily contact with their colleagues was mentioned.

A plea was made for more accommodation to enable mothers to be with their children in the ward. It was felt that a certain number of single rooms should be provided for this purpose.

*Floors.*—Rubber flooring and wood blocks had been found unsuitable. Cork tiling had been found satisfactory in practice.

*Heating.*—Heating by flush wall panels was generally advised.

*Sterilization of crockery.*—It was agreed that crockery should be sterilized centrally, but feeding bottles should be sterilized in the milk room.

*Baths.*—It was suggested that substitution of shower-baths for the ordinary bath might lead to the diminution of infection from this source.

*Ventilation.*—The designs shown provided for ventilation from the corridor through the wards and service rooms. Discussion arose as to whether some form of forced ventilation might not be desirable. It seemed generally agreed that air-conditioning would be unnecessary in such a unit.

The complete duplication of such departments for children in a general hospital would, of course, be expensive. In certain instances where such special departments could not be kept fully employed by a unit of a hundred beds, the provision of such departments would be extravagant. In practice it might be felt difficult to resist the claims of other sections of the hospital to be equipped with complete ancillary services. It may be noted that radiography is more used in Pædiatric Units than in adult units. A possible compromise may be to dedicate a section of the central radiological unit to the children's needs and to train for service in this section radiographers accustomed to dealing with children. A radiologist whose special interests lie in pædiatric radiology may well be given charge of this section of the department.

At this point it is convenient to broach the question of whether the Pædiatric Unit should be structurally separate from the main hospital as it is in some Continental clinics such as Zürich, and as it has now become, to some extent, in certain teaching units in London, for example, St. George's, King's College Hospital and Guy's. The arguments for and against such an arrangement link up with those concerning special ancillary services.

#### STANDARD WARD BLOCK

The standard ward block should consist of a unit of twenty beds, as it is felt that this is the appropriate number for adequate supervision by one sister. From the plans (figs. 1, 2 and 3), it will be seen that this unit provides for the complete isolation of eight patients; the others are nursed in wards containing four beds. Whether such methods of isolation will successfully reduce cross-infection is still debated (Watkins *et al.*, 1946), but in any event it is clear that by reducing the number of beds which have to be closed when infection breaks out more efficient use can be made of the beds available. One of the twenty-bedded units will be dedicated to complete isolation of all patients and in this unit infectious fevers can be nursed.

These plans show, in fig. 1 the relation of a pair of ward units, with the ancillaries common to both, to the general circulation scheme of the hospital as a whole. Fig. 2 shows the lay-out of the individual ward unit of 20 beds. Fig. 3 shows, in axonometric projection, some details of the central part of the ward block.

Within each twenty-bedded unit we have planned :

- (a) Sister's room.
- (b) A milk room.
- (c) A ward kitchen.
- (d) A treatment room.
- (e) A preparation and sterilizing room.
- (f) A nurses' station.
- (g) A sluice room.
- (h) A ward laboratory.
- (i) Clean and dirty linen rooms.
- (j) A woolly-washing room with facilities for drying.
- (k) A lavatory, water-closet and patients' bathroom.
- (l) A day-room.

The functions of most of these are self-evident but the following amplifications may be permitted :

(a) *Sister's room*.—A room for interviewing parents and nurses and to enable sister to put her cap straight.

(c) *Ward kitchen*.—Though most of the cooking will be done in the central hospital kitchen, the preparation of small dishes for young children and infants is a task which must be carried out on the ward and the kitchen facilities, therefore, will have to be appropriate.

(d) *Treatment room*.—It is undesirable that dressings, the giving of anaesthetics and other technical procedures should be carried out in the presence of other children.

(g) *Sluice room*.—The design of the sluice room or utility room illustrates our attempt to avoid cross-infections while employing relatively unskilled nursing staff. It has two doors and traffic passes through the dirty side of the sluice room, where the sluice and bedpan washer are situated and where there should be an incinerator for napkins, to the clean side where sterilized bedpans are stored and where the nurse washes her hands before leaving the room.

(j) *Woolly-washing room*.—Babies' woollies are peculiarly the property of the ward unit and the washing of these woollies should be carried out within the unit.

*Accessory rooms*.—The rooms detailed in the previous paragraph belong exclusively to

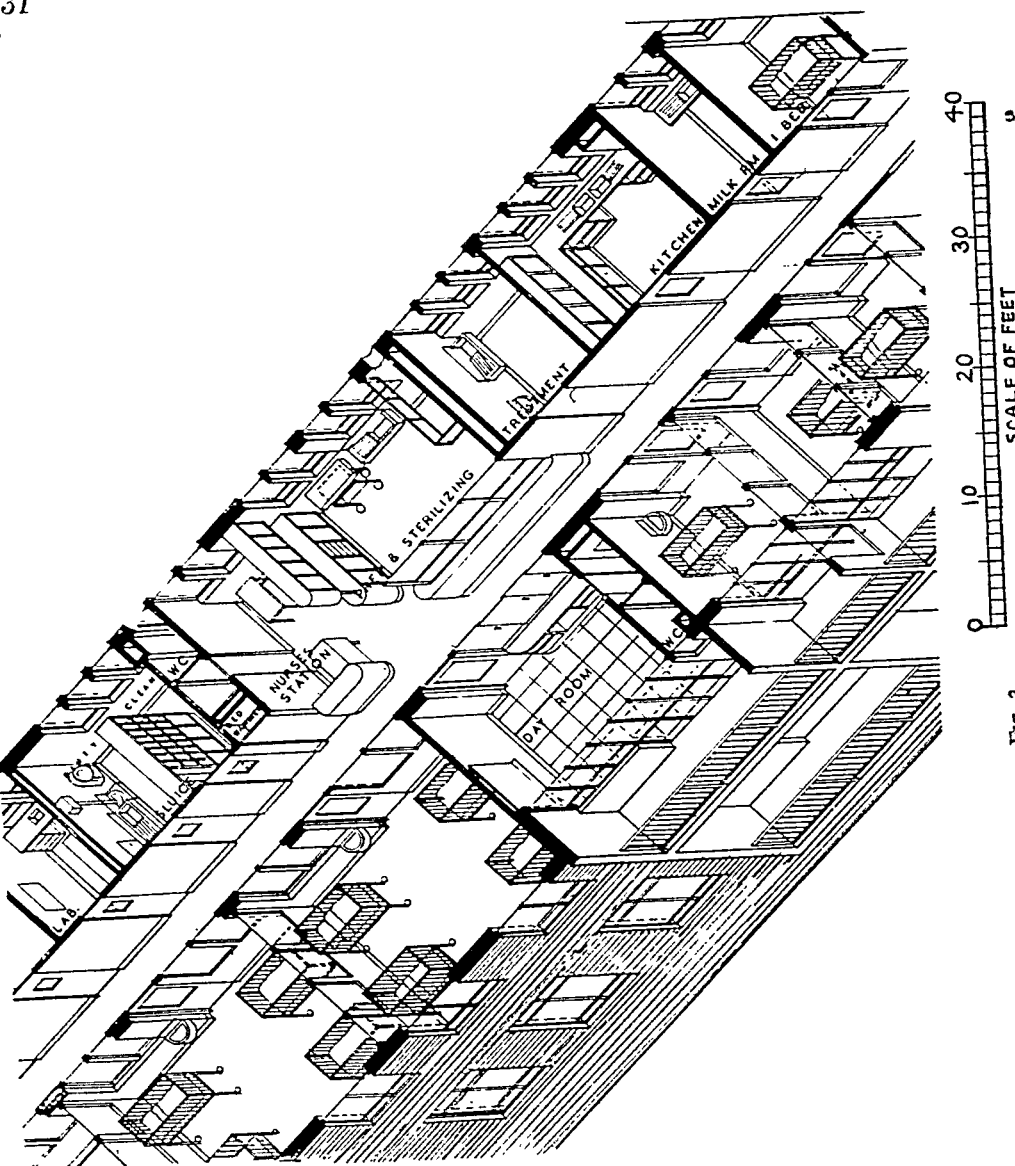


Fig. 3.

FIGURES 2 and 3.

Each unit of twenty beds provides three wards of four beds and eight single bed wards, and has the following ancillary rooms :—

Day-Room  
 Patients' Bath  
 Patients' Lavatory and W.C.s  
 Linen  
 Wool Washing  
 Dirty Linen  
 Ward Laboratory  
 Clean and Dirty Sluices  
 Nurses' Toilet  
 Nurses' Station  
 Preparation and Sterilizing  
 Treatment Room  
 Ward Kitchen  
 Milk Room  
 Sister's Room  
 Store  
 Trolley Bay  
 Balcony

Each pair of units totalling forty beds has the following ancillary and teaching rooms :—

Teaching Room  
 Screening Room  
 Consulting Room  
 Nurses' Cloak-Room  
 Ward Office  
 Visitors' Bedroom  
 Admission Bath and W.C.  
 2 Spare Rooms  
 Visitors' Waiting Bay





into consideration in deciding on the admission of any individual case. Most of the minor disorders and diseases of infancy never reach in-patient hospital practice and there are many other reasons influencing the admission of babies to the hospital. Principal amongst these may be enumerated the availability of beds, the economic and environmental circumstances of the parents and their social background, as well as the type, nature and severity of infant maladies. The resources of the hospital, the interest in, enthusiasm or special facilities for the study and treatment of certain diseases and many other such considerations, all play their part. Another factor, so far as the Birmingham Children's Hospital is concerned, is that the arrangements in the special department for infants are such that approximately equal numbers of cots are reserved for infected cases and for non-infected cases and this segregation of the infants is adhered to strictly. Therefore, the individual admissions must of necessity be regulated and adjusted on this bed distribution basis. It will be appreciated, therefore, that I am dealing with a highly selected group of patients and in consequence my figures will not bear any relationship to the incidence of diseases in the infant population at risk.

With the foregoing reservations in mind, it is now proposed to consider in some detail the incidence, management and mortality of the types of disorder, disease and disability that a children's hospital in a thickly populated industrial area is called upon to treat in infants under 1 year of age. In the first place, the over-all mortality of these 2,306 cases was 37.6, namely 16.3%. If one excludes 120 babies who were very gravely ill on admission, really beyond medical aid and dying within a few hours, the corrected death-rate will be reduced to 11.1%. When it is recollected that fifty years ago the infant mortality in this country was 16.3 per 100 live births, that is of all infants born alive, 80% of whom commence life without any existing disease, a mortality to-day in the same age-group of 16.3% of ill or diseased infants demonstrates very clearly the progress that has been made in infant care.

The cases are divided into two broad groups (a) those admitted suffering from some infection, and (b) those whose disease on admission was not associated with or complicated by any demonstrable infection (Table I).

TABLE I.—INFECTED CASES

|                                  | No. | Deaths | Mortality |
|----------------------------------|-----|--------|-----------|
| Upper respiratory tract .. .. .  | 204 | 12     | 6%        |
| Bronchitis and pneumonia .. .. . | 201 | 56     | 28%       |
| Gastro-enteritis .. .. .         | 176 | 17     | 9.7%      |
| Meningitis (purulent) .. .. .    | 49  | 13     | 26.5%     |
| Tuberculosis (all forms) .. .. . | 27  | 19     | 70%       |
| Skin infections .. .. .          | 26  | 3      | 11.5%     |
| Other infections .. .. .         | 221 | 36     | 16.3%     |
| Total                            | 904 | 156    | 17.3%     |

This list gives only the principal or main site of infection. Many of these babies had, either concurrently or subsequently, evidences of infection elsewhere in the body, but to attempt to detail all these would render the review unnecessarily complicated and confused. As would have been anticipated there is a very high incidence of respiratory and gastro-intestinal infections, indeed two out of every three infants admitted suffering from an infection had an involvement of either the respiratory or the alimentary tract. The clinical association between these two disease syndromes in infancy is very intimate and in an individual case it is often difficult to decide which is the primary aetiological factor. In so far as possible, those infants whose illness appeared to originate with an upper respiratory infection and subsequently developed diarrhoea with or without vomiting, have been included in the former group. It must be admitted, however, that this distinction is somewhat arbitrary, often controversial, perhaps even artificial and not always correct.

Throughout the period under review, chemotherapeutic treatment has been more or less standardized, being based on experience gained in the preceding years (Tables II and III). When *sulphonamide* therapy was employed the large majority of these infants received either *sulphathiazole* or *sulphadiazine*. This must not be taken to imply that these are considered superior to other *sulphonamides*. The reason for their preference was that investigations prior to 1946 had taught their correct dosage to ensure adequate blood concentration. The dosage scheme that has been employed for *sulphathiazole* is 0.25 gramme per pound (0.55 gramme per kilo) of body-weight per day and for *sulphadiazine* 0.15 gramme per pound (0.33 gramme per kilo). It will be noticed that these doses are approximately four or five times the corresponding adult doses, but they are necessary to give and maintain adequate bacteriostatic blood concentrations. With the usual precautions that have been carried out as a routine, toxic phenomena have rarely been encountered and have never been of more than a minor character. Frequent estimations of blood concentrations must, of course, always be carried out when infants are being given these doses, as occasionally a very high level may be reached.

[March 25, 1949]

## A Pattern of Disease in Infancy

Based on 2,306 Hospital Admissions in the Years 1946-48 Inclusive

### PRESIDENT'S ADDRESS

By Professor J. M. SMELLIE, O.B.E., M.D., F.R.C.P.

THE study of infant mortality since universal registration of deaths first established in 1837 has brought to light the principal killing diseases of this period of life. Practical application of this knowledge, coupled with advances in prevention, diagnosis and treatment, has achieved a notable reduction in infant deaths. Whereas at the beginning of the present century the infant mortality rate per 1,000 live births had shown little drop since 1837, it is to-day no more than one-quarter of what it was then. In this connexion, however, it must be emphasized that this reduction has occurred more particularly in the age-period 1-12 months and now more infants die in the first 28 days of life than in the succeeding 11 months. This saving in infant life has been effected particularly by a diminution in the number of deaths from infections. In the quinquennial period, 1896-1900, 25% of infant mortality was due to bronchitis or pneumonia. By the year 1940, this figure had dropped to 12.5%. Gale (1945) has recently analysed the principal causes of infant mortality per 1,000 live births for the period 1931-35. These figures show that premature births accounted for 18, bronchitis and pneumonia 12.2, congenital malformations 5.9 and diarrhoea and enteritis 5.4, the total infant mortality from all causes being 62.3 per 1,000.

Thus, it is clear that knowledge concerning infant mortality is considerable and is still growing. On the other hand, little precise information is available concerning morbidity in this age-period and references in the literature to this aspect of the subject are very meagre. An analysis of the age, sex and seasonal incidence of certain diseases is recorded by Tisdall *et al.* (1930) over a period of five years, one-third of the children having been admitted to hospital. The seven principal diseases of the 509 infants who were under a year of age were: erysipelas 117; intussusception 80; tetany 73; pyelitis 68; eczema 57; retropharyngeal abscess 38; and scurvy 34. Another view-point is presented by Epstein (1931) who reviewed the records of 1,000 consecutive autopsies in children in one hospital over a period of eight years. 548 of these were under 12 months of age and the principal causes of death were: pneumonia 114; tuberculosis 25; septicæmia 23; purulent meningitis 39; prematurity 23; congenital malformations 67; marasmus 34; intoxications 62; and gastro-enteritis 20. He points out that these figures represent incidence in infants who have died and are not comparable with figures of incidence of disease in general.

More recently Collins (1948) in an endeavour to measure the extent of illness among infants under 1 year of age, has analysed the results of a series of periodic canvasses of families living in different parts of the United States of America. These show an illness rate of 1,447 cases per 1,000 years of life: 669 per 1,000 were respiratory, 56 congenital malformations and diseases peculiar to early infancy and 722 due to miscellaneous causes. His tables show that the chief causes of illness among infants are the common respiratory and digestive disorders in contradistinction to the chief causes of mortality which are congenital malformations and the various conditions associated with early infancy.

Birmingham Children's Hospital has a specially designed infants' block, accommodating 60 cots in cubicles, every infant being physically isolated. There are three floors of 20 cots, each staffed by a fully trained sister, a staff nurse and 12 nurses. This building was completed in 1939 but could not come into full use until after the war was over. I propose to base my observations on the patients treated in this block during the years 1946 to 1948 inclusive.

2,306 infants, all under 12 months of age, were admitted in this three-year period. Any infant admitted on more than one occasion for the same complaint (e.g. hæmolytic disease of the newborn) has been counted as a single admission. An analysis of these cases has been attempted in the hope that it will illuminate in some way the type and incidence of the diseases of infancy as now encountered in hospital practice and perhaps focus more attention on this important aspect of child health.

This hospital is the only one in the Midland Region devoted solely to sick children. In consequence it attracts patients from a very wide area and in view of the limited bed accommodation and the great pressure on the beds, many variable factors have to be taken

disease. But as their clinical illnesses were respiratory they have been included in this group. In the older infants, otitis media was a not infrequent complication seen at autopsy.

The majority of the infants who succumbed to *gastro-enteritis* also had an associated mastoiditis, some of which had been recognized and treated during life. The relationship between these two diseases baffles elucidation but does not prevent the postulation of a number of hypotheses and conflicting opinions. As I have stated previously (Smellie, 1939) I cannot subscribe to the view that all cases of infantile diarrhoea are due to parenteral infection, either in the upper respiratory tract or elsewhere. Were this so the curve of incidence of mastoiditis and gastro-enteritis would coincide, but this is contrary to experience. In this country infantile gastro-enteritis does not have any significant seasonal variation, whereas otitis media continues to be much more prevalent in the winter than in the summer months, as shown in fig. 2. At the present time the principles of the treatment of infantile gastro-

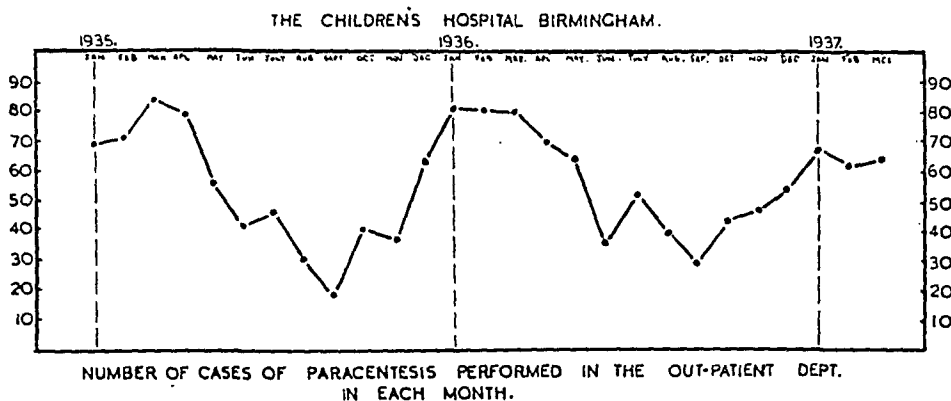


FIG. 2.

enteritis are essentially symptomatic, i.e. the correction of the fluid and electrolytic imbalance by the administration of the appropriate quantity and quality of fluids and salts. Sulphonamides and penicillin have certainly been most valuable therapeutic adjuncts but their success has fallen short of our expectations.

Our experience has confirmed that the prognosis in *meningitis*—excluding tuberculous—depends very largely on the duration of the infection before the introduction of chemotherapy. When the patients are received in the early stage of the disease and intensive therapy instituted the mortality is very low. A mortality rate of 11.5% in *skin infections* is explained by the fact that the 3 fatal cases occurred in babies in the early weeks of life, at a time when it is known that immunological responses are very poorly developed. At this period of life, much more than at any other, measures to prevent infection must not and cannot be relaxed although we have at our disposal so many potent remedies. Prophylaxis must continue to be our watchword.

*Tuberculosis*.—Streptomycin has been available for the treatment of tuberculous meningitis and miliary tuberculosis for about fifteen months. During this period 7 such cases have been treated. 4 were suffering from tuberculous meningitis and all have died. The other 3 were cases of miliary tuberculosis without meningeal involvement; these are responding most satisfactorily, are gaining weight and are very well, but radiologically the pulmonary lesions cannot yet be considered healed.

*Other infections* include genito-urinary infections, non-localized neo-natal infections, osteomyelitis, stomatitis, septicæmia, purulent arthritis, congenital syphilis, &c.

In consideration of an over-all mortality rate of 17.3% in these 904 infected cases, Cruickshank's (1945) observations on infection in infancy are of considerable significance. He has pointed out that the outstanding feature of infection at this period of life is that it is due very largely to bacteria that are endogenous in older children and adults with but little power to initiate infection. Perhaps this may explain, in part at least, why the sulphonamides and penicillin appear to be less efficacious in the infections of infancy.

#### NON-INFECTED CASES

Passing now to those infants whose disease or disability on admission to hospital was not due to or associated with any infection, there is a total of 1,402 with a mortality of 15.7% (see Table V).

TABLE II.—SULPHONAMIDE DOSAGE SCHEME

- (1) Sulphapyridine = 0.25 gramme per lb. (0.55 gramme per kilo) of body-weight per day  
 (2) Sulphathiazole = 0.25 gramme per lb. (0.55 gramme per kilo) of body-weight per day  
 (3) Sulphadiazine = 0.15 gramme per lb. (0.33 gramme per kilo) of body-weight per day  
 (4) Sulphamezathine = 0.15 gramme per lb. (0.33 gramme per kilo) of body-weight per day

All these preparations are dispensed with an equal quantity of sodium bicarbonate.

(1) and (2) to be given at four-hourly intervals, (3) and (4) at four or six hourly intervals.

TABLE III.—TRIPLE SULPHONAMIDE MIXTURE

|                   |    |    |    |    |    |      |
|-------------------|----|----|----|----|----|------|
| Sulphathiazole .. | .. | .. | .. | .. | .. | 0.22 |
| Sulphadiazine ..  | .. | .. | .. | .. | .. | 0.14 |
| Sulphamerazine .. | .. | .. | .. | .. | .. | 0.14 |

Dose = 0.2 gramme per lb. (0.44 gramme per kilo) of body-weight per day.

This preparation is dispensed as a neutral suspension.

During 1946 and part of 1947 *penicillin* was given by intramuscular injection but when investigations (Moseley, 1948) had shown that in infants under 6 months of age adequate blood levels could be attained by oral administration, this latter method has been used except in the presence of severe vomiting or diarrhoea (Table IV, fig. 1).

TABLE IV.—DOSAGE OF ORAL PENICILLIN IN INFANCY

| Age        | 3-hourly     | 4-hourly     |
|------------|--------------|--------------|
| 0-6 weeks  | 20,000 units | 30,000 units |
| 6-12 weeks | 40,000 units | 60,000 units |
| 3-6 months | 50,000 units | 80,000 units |

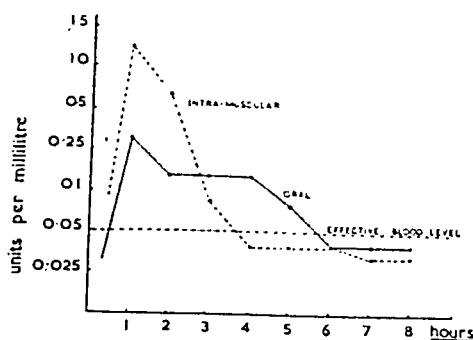


FIG. 1.—Comparison between oral and intramuscular penicillin blood levels in an infant aged 3 months, after 100,000 units.

Other therapeutic measures have conformed to current medical practice, and need no elaboration.

#### COMPARISON OF ADMISSIONS AND MORTALITY OF PRINCIPAL INFECTIOUS DISEASES (see Table I)

*Upper respiratory infections* include a heterogeneous collection of cases whose clinical picture is often complex and confusing. The symptoms may range from a "grumbling" pyrexia of so-called uncertain origin to frank convulsions. The diagnosis may be obvious or only reached after detailed and searching investigations; on the one hand it may be a simple pharyngitis, on the other an occult mastoid infection. This group, which constituted the largest single type of infection dealt with, has a relatively low mortality rate.

A fatality incidence of one in four of infants admitted to hospital suffering from *bronchitis and pneumonia* with complete and comprehensive methods of therapy available is depressing and disturbing. In this connexion, however, it should be explained that the hospital receives these patients from two main sources, the Casualty Department or the general practitioner, and all were seriously ill. Some had not had any treatment, some had had sporadic or inadequate therapy and some had failed to respond to really good treatment. Clearly, there is an urgent necessity for further research and investigation into this problem. Prophylaxis must, of course, come first and here good hygienic surroundings, good nutrition and a keen appreciation of the risks of infection are points to emphasize. Recognition of the disease in the earliest possible stage, a realization of its gravity and the prompt institution of therapy based on present knowledge would, I am sure, achieve a significant reduction in the death-rate. Post-mortem examination of the fatal cases showed that complications of one kind or another were almost invariably present. In those dying in the neo-natal period intracranial hæmorrhage of minor or major extent was found in many, so perhaps here the pneumonia might more correctly be described as a complication than as the original

these patients belong to a highly selected group and are very far from being a representative composition of this disease. One died of bacterial pneumonia but in the remaining 8 the cause of death was haemorrhage. 5 of these were premature infants, all of whom were given 20-30 cc. of blood within a few hours in spite of immediate blood transfusion and other resuscitative measures. In 4 there was massive pulmonary haemorrhage and in 2 others the main site of the bleeding was the gastro-intestinal tract. None of these infants had any haemorrhagic haemorrhage; none had received any vitamin K. All except 1 died within six to eighteen hours of admission. One premature infant lived for six days but vitamin K and blood transfusions failed to control the haemorrhage and at autopsy the gastro-intestinal tract was almost filled with blood. It cannot be questioned that vitamin K has reduced both the morbidity and the mortality of haemorrhagic disease of the newborn to a very significant extent, more particularly as a prophylactic, but there remain some cases where the bleeding is not controlled. In such there must be a deficiency or disturbance of factors additional to prothrombin but what these may be is not yet known. Deficient fibrinogen may be a factor in some of these.

It is an interesting and most pleasing reflection on the overwhelming success of the propaganda against the vitamin deficiency diseases that no case of rickets that may have been seen was sufficiently severe to necessitate in-patient treatment and there were only two cases of scurvy. One of these has an interesting moral that we are sometimes apt to overlook, namely, that disease must not be treated to the neglect of the patient. This was an infant of 9 months of age, who, six months previously, had developed eczema. This responded very satisfactorily to a soya bean preparation which his mother kept him on to the exclusion of every other food or supplement. On admission he had well-marked clinical signs of scurvy associated with a mild rickets. On a mixed diet and vitamin therapy a cure was soon effected without any recurrence of the eczema.

*Other congenital abnormalities.*—These are a heterogeneous collection of congenital malformations with an inevitable death in many, hence the high mortality rate. Included in these were congenital heart disease, 23 cases; fibrocystic disease of the pancreas, 19; congenital malformations of the esophagus, 8; meningocoele, 11; and duodenal or intestinal obstruction, 18.

## DISCUSSION

One of the principal reasons that led me to undertake this survey was that in Birmingham we are fortunate to have a special unit accommodating 60 infants on the cubicle system. This building was designed shortly before the war and incorporated all the latest ideas. So far as I am aware, there is no other comparable hospital accommodation of this size and character in this country. It was felt, therefore, that we in Birmingham had a duty to let others know what our experiences have been and thereby perhaps contribute something to the welfare of the infant population as a whole. With the number of cots that are available a three-year period has provided a sufficiently large number of cases to enable some assessment to be made of the results that are being obtained.

Appreciating the selection and limitation in type and character of the cases with which I have been dealing, it may be of interest to compare the diseases that necessitated admission to hospital with those that were fatal (Tables VI and VII).

In both groups *congenital abnormalities* occupy a prominent position, and in the present state of knowledge a high mortality must be accepted, but recent advances in surgical treatment are opening up new approaches. The problems of *nutrition and feeding* are coming under control and the treatment of *pyloric stenosis* is producing brilliant results. On the other hand, *respiratory and pulmonary infections* and the so-called *diarrhoea and vomiting syndrome* remain still as major problems. Paediatricians have been rebuked (Cruickshank, 1945) for being too much concerned with infection in the individual child and not enough with infection in the child community. We must take up this challenge. The quickly advancing knowledge concerning *haemolytic disease of the new-born* should soon bear fruitful results with a diminution in both incidence and mortality.

It is now generally realized that the admission of an infant to hospital carries grave responsibilities, with considerably increased risks of contracting infection of one kind or another unless very special precautions are adopted. Indeed, it has been claimed in some quarters that however strict and careful may be the practice in hospital to combat these risks, they remain a very real and more or less unsurmountable problem. In consequence some have urged that in-patient treatment for infants should be reserved exclusively for the comparatively small number who literally cannot, even under good circumstances, obtain the requisite treatment in their own homes. I do not know of any figures relative to the mortality of a comparable series of ill infants treated in their own homes with those treated

TABLE V

|                                                     | No.   | Deaths | Mortality |
|-----------------------------------------------------|-------|--------|-----------|
| Pyloric stenosis. . . . .                           | 330   | 7      | 2.1%      |
| Feeding problems (including simple marasmus) . .    | 200   | 1      | 0.5%      |
| Hare-lip and cleft palate . . . . .                 | 111   | 6      | 5.4%      |
| Hæmolytic disease of newborn . . . . .              | 86    | 22     | 25.6%     |
| Prematurity . . . . .                               | 80    | 34     | 42.5%     |
| Birth injuries . . . . .                            | 40    | 13     | 32.5%     |
| Pink disease . . . . .                              | 31    | 4      | 12.9%     |
| Intussusception . . . . .                           | 30    | 4      | 13.3%     |
| Hæmorrhagic disease of newborn . . . . .            | 30    | 9      | 30%       |
| Hæmolytic and nutrition anæmia of later infancy . . | 24    | 2      | 8.3%      |
| Scurvy . . . . .                                    | 2     | 0      | 0%        |
| Other congenital abnormalities . . . . .            | 268   | 101    | 38.0%     |
| Unclassified . . . . .                              | 170   | 17     | 10%       |
|                                                     | 1,402 | 220    | 15.7%     |

## COMPARISON OF ADMISSIONS AND MORTALITY OF PRINCIPAL NON-INFECTED CASES

*Pyloric stenosis.*—One out of every seven infants admitted to the Birmingham Children's Hospital during the last three years has been suffering from pyloric stenosis, or, if we exclude those suffering from infection, one out of four. There are several possible explanations for this relatively large number, which have already been mentioned.

According to Davison (1946) pyloric stenosis has an incidence in this country of 3 per 1,000 live births. In England and Wales there were 886,800 live births in 1947, giving a total incidence of pyloric stenosis of 2,660; in Birmingham there are about 23,000 live births each year and this would account for about 70 cases.

It will be seen that our mortality rate is 2.1%. 6 of these deaths occurred in 1946, there were no deaths in 102 cases in 1947 and only 1 death—in a very marasmic infant—in 1948. Thus out of 207 cases treated in 1947–48 there was only one death, that is the mortality rate was under 0.5%. In over 99% of these cases the treatment was surgical. Appreciating that pyloric stenosis successfully treated gives a complete recovery and failing treatment many infants must succumb, the early diagnosis and facilities for up-to-date treatment are of paramount importance. The case mortality in this country is about 16% and may be even higher (Davison, 1946); a reduction of this figure to 1% or less would be a great achievement which we should be able to attain, with, it may be emphasized, complete and permanent restoration to health.

"*Feeding problems*" is a term which has been used to cover a rather vague and ill-defined group of infants admitted with a variety of suspected ailments, e.g. pyloric stenosis, pylorospasm, marasmus, fibrocystic disease of the pancreas, &c. All were under weight and a number were definitely marasmic. Detailed observation and investigation failed to reveal any evidences of organic disease and treatment demonstrated that the fault lay with the feeding and general management rather than with the infant. During the period with which I am concerned, an investigation into the feeding of marasmic infants on a high protein diet was proceeding (Smellie, 1948). The feeds that were used provided approximately 60 calories and 3 grammes of protein per pound (6.6 grammes per kilo) of body-weight per day. Such infants tolerate these feeds well and their general progress and weight gain was very satisfactory; they seemed to do better on these augmented feeds.

*Hæmolytic disease of the newborn.*—These 86 infants were admitted at varying ages and stages of their illness. Some were only a few hours old and were known or suspected cases admitted for observation and treatment if required. Others were only received after several days and some were already gravely ill. The general scheme of treatment that has been carried out during the period under review was, in the presence of an anæmia of 70% or more, transfusions of the appropriate quantity of Rh-negative blood to restore the hæmoglobin to 90–100%. Our present practice is to give the blood by the "shot" method directly into a scalp or other superficial vein and only exceptionally is the "drip" technique employed. Experience has taught that 80 or even 100 c.c. of blood can safely be given at one time, provided the injection is given slowly, the time allowed being twenty to thirty minutes. When more than this amount is needed to restore the hæmoglobin to a satisfactory level, an interval of four to six hours is allowed to elapse before the second injection. In some cases packed cells have been used. In no case has a replacement transfusion been given. The case mortality of this series was 25.6%. Kernicterus was demonstrable in 18 out of 22 fatal cases, 2 showed some biliary cirrhosis, and the remaining two died of neo-natal infections.

*Hæmorrhagic disease of the newborn.*—A death-rate of nearly one in three of infants suffering from hæmorrhagic disease of the newborn deserves some comment, bearing in mind that

# PROCEEDINGS *of the* ROYAL SOCIETY OF MEDICINE

ISSUED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE

HONORARY EDITORS

ERIC A. CROOK      E. R. CULLINAN

EDITOR

J. M. BROWNE KUTSCHBACH

|                                           |                                 |
|-------------------------------------------|---------------------------------|
| G. S. W. ORGANE (Anæsthetics)             | F. T. RIDLEY (Ophthalmology)    |
| J. S. RICHARDSON (Clinical)               | H. L.-C. WOOD (Orthopædics)     |
| J. B. BROOKSBY (Comparative Medicine)     | C. S. HALLPIKE (Otology)        |
| E. W. PROSSER THOMAS (Dermatology)        | A. G. SIGNY (Pædiatrics)        |
| E. F. SCOWEN (Endocrinology)              | F. R. SELBIE (Pathology)        |
| ALLAN McFARLAN (Epidem. & State Med.)     | M. B. RAY (Physical Medicine)   |
| A. C. WHITE (Exper. Med. & Therap.)       | O. V. LLOYD-DAVIES (Proctology) |
| I. E. McCracken (History of Medicine)     | DENIS HILL (Psychiatry)         |
| W. A. MILL (Laryngology)                  | F. CAMPBELL GOLDING (Radiology) |
| MAURICE DAVIDSON (Medicine)               | CHARLES DONALD (Surgery)        |
| J. St. C. ELKINGTON (Neurology)           | G. M. FINDLAY (United Services) |
| LESLIE WILLIAMS (Obstetrics & Gynæcology) | A. CLIFFORD MORSON (Urology)    |
| B. W. FICKLING (Odontology)               |                                 |

SECRETARY OF THE ROYAL SOCIETY OF MEDICINE

G. R. EDWARDS

TABLE VI.—EIGHT PRINCIPAL DISEASES IN INFANTS ADMITTED TO HOSPITAL (C. H. B. 1946-48)

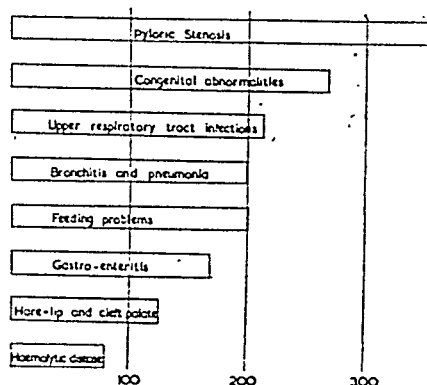
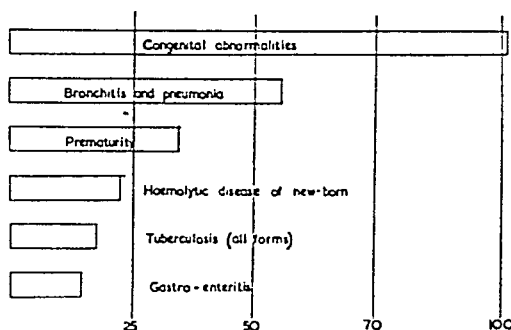


TABLE VII.—SIX PRINCIPAL FATAL DISEASES OF INFANTS IN HOSPITAL (C. H. B. 1946-48)



in hospital but I am very conscious of the difficulties, the trials and the tribulations that mothers of infants and children have to overcome in their homes in a thickly populated industrial area in England to-day. I find it difficult to believe that a mortality rate of seriously ill babies in such an environment is less than the 11.1% which has been the experience of the Birmingham Children's Hospital. It would not surprise me if it were very much more.

## REFERENCES

- COLLINS, S. D. (1948) *Publ. Hlth. Rep. Wash.*, 63, 640.  
 CRUICKSHANK, R. (1945) *Arch. Dis. Childh.*, 20, 145.  
 DAVISON, G. (1946) *Arch. Dis. Childh.*, 21, 133.  
 EPSTEIN, I. M. (1931) *Amer. J. Dis. Childh.*, 41, 1363.  
 GALE, A. H. (1945) *Arch. Dis. Childh.*, 20, 2.  
 MOSELEY, J. H. (1948) *Arch. Dis. Childh.*, 23, 93.  
 SMELLIE, J. M. (1939) *Lancet* (i), 969.  
 — (1948) *Arch. Dis. Childh.*, 23, 98.  
 TISDALL, F. F., *et al.* (1930) *Amer. J. Dis. Childh.*, 39, 163.



# PROCEEDINGS

## OF THE

# ROYAL SOCIETY OF MEDICINE

Vol. XLII    No. 9    September 1949

## CONTENTS

Whole  
Proceedings  
Page

### Section of Endocrinology

|                                                                                                                               |     |
|-------------------------------------------------------------------------------------------------------------------------------|-----|
| Treatment of Undescended Testicle.—DENIS BROWNE, F.R.C.S. . . . .                                                             | 643 |
| Fertility in Operatively Treated and Untreated Cryptorchidism.—T. SVEND HANSEN, M.D., <i>Copenhagen</i> . . . . .             | 645 |
| Investigations on the Endocrine Function of the Testicle in Cryptorchidism.—HARALD ENGBERG, M.D., <i>Copenhagen</i> . . . . . | 652 |

### Section of Surgery

*April 6, 1949*

|                                                             |     |
|-------------------------------------------------------------|-----|
| DISCUSSION ON RESECTABLE CARCINOMA OF THE STOMACH . . . . . | 659 |
|-------------------------------------------------------------|-----|

*May 4, 1949*

MEETING AT NORTH MIDDLESEX HOSPITAL, SILVER STREET, LONDON, N.18.

|                               |     |
|-------------------------------|-----|
| List of Cases Shown . . . . . | 672 |
|-------------------------------|-----|

### Section of Otology

|                                                                            |     |
|----------------------------------------------------------------------------|-----|
| Recent Developments in Auditory Tests.—S. RICHARD SILVERMAN, Ph.D. . . . . | 675 |
|----------------------------------------------------------------------------|-----|

### Section of Epidemiology and State Medicine

|                                                                                              |     |
|----------------------------------------------------------------------------------------------|-----|
| "I Remember".—President's Address by Sir ALLEN DALEY, M.D., F.R.C.P., D.P.H., K.H.P. . . . . | 687 |
|----------------------------------------------------------------------------------------------|-----|

### Section of Anaesthetics

|                                     |     |
|-------------------------------------|-----|
| ANÆSTHETIC RESPONSIBILITY . . . . . | 697 |
|-------------------------------------|-----|

### Section of Comparative Medicine

|                                       |     |
|---------------------------------------|-----|
| DISCUSSION ON LEPTOSPIROSIS . . . . . | 707 |
|---------------------------------------|-----|

### Section of the History of Medicine

|                                                                                            |     |
|--------------------------------------------------------------------------------------------|-----|
| The History of Research upon the Renal Circulation.—K. J. FRANKLIN, D.M., F.R.C.P. . . . . | 721 |
|--------------------------------------------------------------------------------------------|-----|

### Section of Physical Medicine

|                                                                                    |     |
|------------------------------------------------------------------------------------|-----|
| DISCUSSION ON THE SIGNIFICANCE OF PATHOLOGICAL TESTS IN RHEUMATIC DISEASE. . . . . | 731 |
|------------------------------------------------------------------------------------|-----|

### Section of Obstetrics and Gynaecology

*March 18, 1949*

|                                                                                                                                                             |     |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|
| Obstetric Analgesia: A New Machine for the Self-Administration of Nitrous Oxide—Oxygen.—E. H. SEWARD, M.A., B.M., B.Ch.Oxon., D.A., D.Obst.R.C.O.G. . . . . | 745 |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|

*May 20, 1949*

|                                                                 |     |
|-----------------------------------------------------------------|-----|
| DISCUSSION ON THE TREATMENT OF CARCINOMA OF THE VULVA . . . . . | 747 |
|-----------------------------------------------------------------|-----|

*(Continued on next page)*



# MALE HORMONE

ROUSSEL

---

**TAB. METHYLTESTOSTERON. B.P.**  
Glosso-Sterandryl—5, 10 and 25 mg.

**IN J. TESTOSTERON. PROP. B.P.**  
Sterandryl—5, 10, 25, 50 and 100 mg.

**IMPLANT** of 100 mg. TESTOSTERONE  
Sterandryl—Implant.



ROUSSEL LABORATORIES LIMITED  
4, Golden Square, London, W.1  
GERard 3111-2

## Section of Endocrinology

President—H. GARDINER-HILL, M.B.E., M.D., F.R.C.P.

[February 23, 1949]

### Treatment of Undescended Testicle

By DENIS BROWNE, F.R.C.S.

*Surgeon to the Hospital for Sick Children, London*

*Diagnosis.*—It is well known to all who have studied the subject that "Undescended Testicles" are about four times as common among young boys as among young adults (both groups being untreated), in other words, that in about 80% of these cases the testicles descend spontaneously before full development is reached. One might expect therefore that an attempt would have been made to separate the organs that would spontaneously descend from those that would not, and so divide the cases into two different groups, those of delayed but ultimately normal development, and those of congenital abnormality. As the question is one of anatomy, one might also have supposed that the normal structure of the parts concerned during development would have been studied, and divergencies from it carefully classified.

It was strange, therefore, to find, when I began to study the subject, that textbooks of anatomy gave no account of the very interesting variations of position and range of movement in the adolescent testicle, and that methods of diagnosis were confined either to waiting to see what happened or to trying the effect of a method of treatment (the injection of hormones).

My investigations of the anatomy convinced me that there was one fundamental error in all the writings I found; the notion that if a testicle moved out of the scrotum upwards over the pubic bone it went into the inguinal canal, and that testicles felt above the pubis were in the canal also. It seems to have occurred to nobody that such a structure in the canal would be under the tendon of the external oblique, and in consequence would become less palpable if that muscle contracted; all these testicles on the contrary then became more easily palpable owing to the tenseness of the muscle giving a rigid backing against which they stood out. Where they actually went to was interesting. I found it was into an abdominal extension of the scrotum, between the fascia of Scarpa and the external oblique, directly over the inguinal canal: I called this the superficial inguinal pouch.

Now, as I have found out in several other cases of the same kind, the difficulty of getting corrections of classical textbook anatomy accepted by anatomists is almost insuperable. Apart from requiring them to admit that they have been teaching what is demonstrably incorrect, there is the examination system to be considered. Unless the change were to be made simultaneously in all schools, those students taught by a holder of the new opinion might be failed in an examination by one who clung to the old: and there is no way of getting such heresy either confirmed or confuted. The surgeons are loth to move without the authority of the anatomists, and in consequence one must be content with a simple absence of comment, and take it that silence means consent.

It may be noted that the variety of maldevelopment that misleads surgeons is that which I have called the emergent testicle, in which the organ may be felt in the superficial inguinal pouch when the child is examined, and then found in the inguinal canal at operation when the muscles are relaxed, and the body recumbent. It is concluded, unless the parts are carefully investigated, that the testicle when felt was in the same position as when exposed, although it has actually followed a course much the shape and length of a hairpin in between.

Once the anatomy of the region concerned is grasped, it is possible to separate the cases sent up by the Profession for opinion into 80% of retractile testicles, as I call those which range from high or low in the scrotum into the superficial inguinal pouch, and another group of 20% of congenital deformities. These include the true undescended testicles, in which the organ cannot be brought down over the bar of the pubic bone, and the various forms of ectopia. The commonest of these, the inguinal ectopic testicle, is shown as an "undescended testicle" in almost all illustrations of the operation for this condition. The finding of a testicle and the ascertaining of its full range of movement downwards may be far from easy in certain cases, particularly those with excessive fat and the tiny gonads typically found in early male obesity. The trick is to force it down with one hand from above, while catching it from below with the other. I have found that diagnosis by physical examination is the only reliable method, just as it would be in any other question of the kind elsewhere

## Section of Ophthalmology

|                                                                           |     |
|---------------------------------------------------------------------------|-----|
| Ocular Defects in Still's Disease.—H. E. HOBBS, F.R.C.S...                | 755 |
| Multiple Congenital Anomalies of the Eyes.—A. J. BALLANTYNE, M.D. Glasgow | 756 |

(N.B.—The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.)

**Copyright:** The Society holds the copyright of all matter accepted for publication in the *Proceedings*. Requests for subsequent publication elsewhere should be made to the Honorary Editors. All papers, &c., presented at meetings (other than those which have been previously published) are held to be subject to the Society's copyright until a decision in regard to their publication has been made.

**Digests:** Requests for permission to make Digests from the *Proceedings* should be addressed to the Honorary Editors.

All communications concerning Editorial Business should be addressed to  
THE HONORARY EDITORS, 1, WIMPOLE STREET, LONDON, W.1

Applications for advertisement space in the "*Proceedings*" should be made to the Society's official advertising agents, Messrs. C. Mitchell & Co. Ltd., Mitchell House, 1 and 2, Snow Hill, London, E.C.1.

Copies of the whole *Proceedings* may be purchased through any bookseller. Prices are as follows:—

|                                                                     |                           |
|---------------------------------------------------------------------|---------------------------|
| Single copies .. .. .                                               | 10s. 6d. each, post free. |
| Annual subscription, covering 12 monthly issues and annual index .. | £6 6s. 0d.                |

Reprints of Sectional parts may be obtained direct from the Society. Prices are as follows:—

|                             |                          |
|-----------------------------|--------------------------|
| Single copies .. .. .       | 3s. 6d. each, post free. |
| Annual subscription .. .. . | 15s. 0d.                 |

Fellows and Members of the Royal Society of Medicine are asked to apply direct to the Society for any copies of the *Proceedings* they may require, whether whole or Sectional, in addition to those they receive gratis. Prices are as follows:—

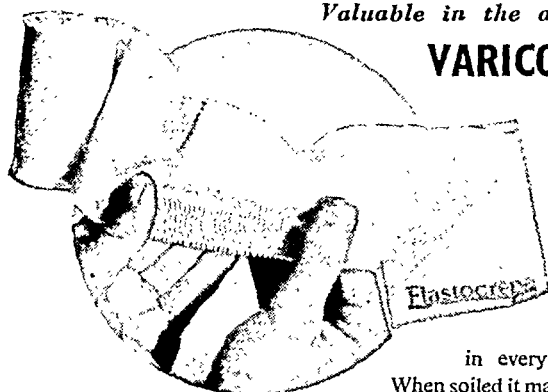
**Whole *Proceedings*:**

|                                                              |                          |
|--------------------------------------------------------------|--------------------------|
| Single copies .. .. .                                        | 7s. 6d. each, post free. |
| Complete volume (12 monthly issues and annual index) .. .. . | £5 0s. 0d.               |

**Sectional *Proceedings*:**

|                             |                          |
|-----------------------------|--------------------------|
| Single copies .. .. .       | 3s. 0d. each, post free. |
| Annual subscription .. .. . | 10s. 0d.                 |

Valuable in the after-treatment of

**VARICOSE VEINS & ULCERS**

Elastocrepe is Elastoplast cloth without the adhesive spread. It therefore, has the unique properties of *stretch* and *regain* which are associated with Elastoplast.

Elastocrepe provides comfortable and adequate support and compression for its particular purpose, and is superior

in every way to the ordinary crepe bandage.

When soiled it may be washed—washing *renews* its elasticity.

**Elastocrepe** SMOOTH SURFACE COTTON CREPE BANDAGE

TRADE MARK

Made in England by T. J. SMITH & NEPHEW LTD., HULL

As to the treatment of the retractile testicles, my own practice is to leave them alone to descend as and when they will, reserving hormone treatment for such cases as show a lack of these substances by obvious sexual underdevelopment. There is a tendency to talk of a course of hormone injections as if it were a trivial matter which, if it does no good, can at any rate do no harm. In my experience most children dread a course of injections intensely, and I should say that as a general rule it has more mental effect upon them than an operation with proper premedication. Apart from this there has been a strange lack of discussion on the effects of the various substances used upon the cells of the testicle.

It is not enough to say that there is no danger when the treatment is given by a competent endocrinologist; far the greater number of these injections are given by general practitioners and they are not warned about the dangers of them. Any medical practitioner knows there are limits to the amounts of thyroid or adrenal extract that can be safely injected, but it is quite a new idea to many that a testicle may be atrophied by certain gonadotrophic substances in certain doses. Yet I have seen several cases in which I am sure this testicular atrophy has occurred.

There has been a tendency lately to shift the indications for hormone treatment from anatomy to psychology, on the grounds that boys may develop complexes about their virility if their testicles are not constantly in the adult position, or that they may be exposed to jeers from their contemporaries on the same account. My own experience of these cases is now large, and I can say that I have never known a boy express anything but relief on being told that his testicles merely needed leaving alone. As to the second point, in the course of various athletic and military pursuits I have been among groups of unclothed males of different ages, nationalities, and social status, and among them all comments upon the genitalia would have been regarded with general disapproval. I do not say that jeers of this sort never occur, but if they do they are rare. In any event their frequency would have an interesting relation to the temperature, as in most small boys and many adults a cold swim will cause the testicles to retract into the abdominal portion of the scrotum.

#### REFERENCES

- BROWNE, DENIS (1933) Some anatomical points in the operation for undescended testicle, *Lancet* (i), 460.  
 — (1938) The diagnosis of undescended testicle, *Brit. med. J.* (ii), 168.

## Fertility in Operatively Treated and Untreated Cryptorchidism

By T. SVEND HANSEN, M.D., *Copenhagen*

IN 1925 Williams and Savage proved the existence of a correlation between fertility in bulls and the occurrence of abnormally formed spermatozoa in their ejaculates. As a result of these discoveries, this problem was also considered in connexion with the fertility of human beings—first by the American gynaecologist Moench, whose work appeared in 1927.

In the following years sperm examinations were made by numerous investigators all over the world, and a variety of literature is now available on the subject; I shall, however, not go into this at any length, except so far as concerns the information which at present we consider obtainable by the examination of human sperm.

From the now numerous sperm examinations available of men who must be presumed to be normally fertile, knowledge has been gained of the limits within which lie what we might call the "normal figures", and, furthermore, of other figures to which we should attach significance.

These are: the amount of semen—which is normally above 2 c.c.; the number of spermatozoa per c.c.—normally exceeding 60 million, on an average from 80 to 150 million—and the percentage of spermatozoa with abnormally shaped heads, which is usually below 20%; finally the number of motile spermatozoa and the degree of motility.

The intimate knowledge now gained of the composition of human semen and of the histopathology of spermatozoa provides an important means of estimating male fertility. The method of examination has been found very useful clinically for investigating sterility

in the body. Why it has been so neglected in the past is inexplicable; one is tempted to suggest the influence of a sexual taboo in the region. In the great majority of cases diagnosis is easy, but I have made mistakes in trying to distinguish between those testicles which will come just into the neck of the scrotum and those which will not; the average of error, however, should be well under 1% of cases investigated (Browne, 1938).

It is, as I have mentioned, often suggested that hormones should be used as a method of diagnosis, and operation advised if they do not work. I have found the action of hormones most unreliable in this regard, and have often seen retractile testicles which I should unhesitatingly class as normal refuse to respond to them by taking up the adult position.

*Treatment.*—We now have divided the mass of boys who are classed by the profession in general as having "undescended testicles" into 80% with delayed but normal development, or retractile testicles, and 20% with congenital deformities, either ectopia or true incomplete descent. There is no argument that for this second class surgery is the only remedy, but the results of surgery at present are far from satisfactory: I think that the frequency of testicular atrophy after operation needs far franker recognition and fuller investigation than it has yet had.

In my opinion all operations hitherto advised have two fallacies in them. The first is anatomical, in that there is no account in classical anatomy of the suspension of the testicle. I have gone into this elsewhere (Browne, 1933), and will merely point out that I have stated, without being refuted, that the internal spermatic fascia of the anatomists does not exist, and that the fibres described in accounts of the surgery as "adhesions" are in fact a definite structure whose deliberate exposure and division is the key to the liberation of the organ.

The second fallacy is physiological, and turns on the tendency of blood-vessels to go into spasm if stimulated in certain ways. The transplantation of the testicle at the end of the long spermatic cord is very comparable to the shifting of a caterpillar skin graft. No one would expect success if this were done in such a way as to put tension upon the tube of skin, and in consequence on the vessels supplying the far end: yet all operations for transplanting the testicle into the scrotum put, by one device or another, tension upon the cord. I have devised a method of fixing the testicle in the scrotum by an anatomical lock, not merely by adhesions, and so leaving it there free from tension upon the vessels, and yet unable to retract upwards. There is no space here to describe the method in full, but fig. 1 shows an outline of it.

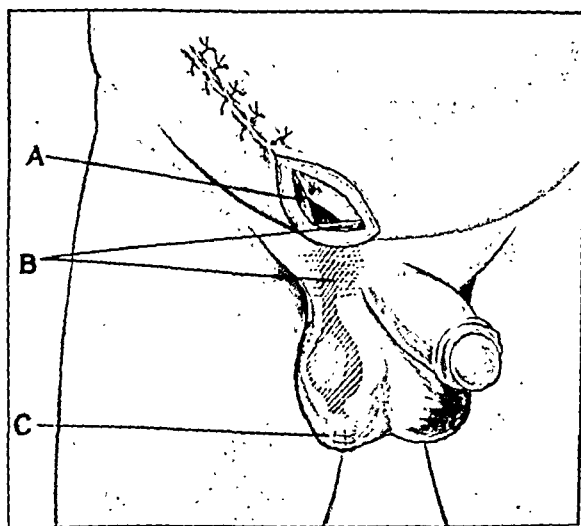


FIG. 1.—*Fixation of a testicle in the scrotum.* If the skin over the pubis is raised by lifting a self-retaining retractor in the wound a tunnel will appear leading into the scrotum along the course the testicles should normally follow. On the floor of this tunnel, between it and the pectineus, is a band of loose but strong and firmly fixed fascia. The testicle is pulled under this and then left free in the loose tissue of the upper part of the scrotum, with no attempt to drag it down to the full extent of the cord. (A) Reconstituted external ring. (B) Band of fascia under which testicle has been pulled. (C) Incision in scrotum through which testicle has been pulled into position.  
(Drawing by Miss Aletta Lewis.)

Examinations of semen from 9 of these patients revealed aspermia, that is, sterility in all the cases, as might have been expected. These examinations are only mentioned as a formality; they illustrate the well-known fact that abdominally- or inguinally-placed testes do not produce spermatozoa; consequently such patients are sterile.

Group B comprises patients with operatively treated bilateral cryptorchidism and consists of the following: 22 patients treated with bilateral orchidopexy; 4 patients treated with unilateral orchidopexy, while the other testis is situated in the abdomen or in the inguinal canal; 3 patients treated with unilateral orchidopexy, the other testis having been placed intraperitoneally during the operation; finally 1 patient treated with unilateral orchidopexy, while the other testis has been removed.

Thus Group B comprises 30 cases of bilateral cryptorchidism, where by means of orchidopexy the transfer of one or both testes to the normal position in the scrotum has been attempted. In the cases where only a unilateral orchidopexy has been made, the other testis has either been removed or is situated in such a place that we must take it for granted that it does not contain spermatogenetic tissue.

By examining the semen of these men it is possible to ascertain the spermiogenic function of testes treated with orchidopexy; but we must remember that by semen examination we cannot decide whether a possible aspermia is due to lack of spermatogenetic tissue in the testes, or whether spermatozoa are produced which cannot be ejaculated on account of an occlusion of the efferent spermatic ducts. This is, however, of no consequence in estimating fertility.

The origin of any aspermia discovered can only be decided by a histological examination of testicular tissue after a biopsy.

I succeeded in obtaining semen for examination from 25 of these patients and the evaluation of their fertility, made in the way described, is shown in fig. 1.

It will be seen that aspermia, that is, sterility, was found in 14 cases, and only in 2 patients was there no sign of impairment of fertility, while the remaining 9 patients showed signs of a more or less marked impairment.

Some of the results of the individual parts of the sperm examinations are shown in the following table:

| <i>Number of spermatozoa per c.c.</i> | <i>Cases</i> | <i>Differential count</i>         | <i>Cases</i> |
|---------------------------------------|--------------|-----------------------------------|--------------|
| Aspermia .. .. .                      | 14           | 20% of abnormal heads and less .. | 5            |
| Less than 1 million per c.c. ..       | 2            | 21 to 30% of abnormal heads ..    | 1            |
| 1 to 10 million per c.c. ..           | 2            | 31 to 80% of abnormal heads ..    | 4            |
| 10 to 50 million per c.c. ..          | 7            |                                   |              |

In one case the number of spermatozoa was so small that a differential count could not be made. Furthermore, these figures show that in none of the cases do we find normal average values in all the individual parts of the examination.

These results, which must be regarded as rather unsatisfactory, form a striking contrast to those which are said to follow from treatment with orchidopexy when only the anatomical outcome is considered.

It might now be imagined that mainly patients with bad anatomical results had accepted my invitation to appear at the follow-up examination, but this is not the case.

At an earlier date, in 1935, these patients had been examined (with others) as to the anatomical result by another Danish surgeon, Dr. Bjerre, who reported the following:

|                                                      |       |
|------------------------------------------------------|-------|
| Anatomically normal and satisfactory results .. .. . | 60.3% |
| Unsatisfactory results .. .. .                       | 30.9% |
| Atrophy .. .. .                                      | 8.8%  |

The result of Bjerre's investigations—which comprised 81 patients operatively treated for bilateral cryptorchidism, with a total number of 136 operated testes—is on the whole in accordance with the results found by other investigators.

To summarize, 25 of these patients, with 43 operated testes, are included in my material (Group B), and the anatomical results of the operation have been estimated by Bjerre as 51.1% anatomically normal and satisfactory; 37.2% unsatisfactory; 11.6% atrophy.

Thus, if we compare results in my small group with those in the much larger group originally investigated, it will be seen that no selection of severe cases has been made in mine.

Besides examining the fertility of these patients I have of course also estimated the anatomical result.

Most investigators base their judgment chiefly on the size and position of the testis—but this is not sufficient. The consistency of the testes must also be considered.

in marriage. Sperm investigations are now an indispensable link in the chain of examinations employed in these cases.

But sperm examinations have also attained great importance within other fields of clinical medicine; for instance in the follow-up of patients who have been operated on for cryptorchidism. It had been realized that such examinations were needed for a final assessment of the therapeutic results but at that time we lacked the method of sperm examination now at our disposal. Only a few cases of examination of sperm from patients who had undergone orchidopexy have been reported by the earlier investigators. In the literature I have found only one work—published in 1935 by MacCollum—in which examination of a considerable number of patients has been made, but it consisted only of counts of the spermatozoa, and accordingly these records are of limited value.

Thus in 1942, when I started my investigations at the University Institute of Forensic Medicine in Copenhagen, few results were available of patients surgically treated for cryptorchidism; moreover, in these follow-up examinations the fertility of the patients as judged by sperm investigations carried out by a reliable technique had not been taken into account.

The problem which I have tried to solve is the correct evaluation of the results of orchidopexy by means of sperm examinations. It was my opinion that a revision was needed of the numerous earlier investigations in which the evaluation of the outcome had been based upon the anatomical result, as I believe that the operation can only be said to have achieved a satisfactory result if fertile spermatozoa are found.

On the whole little value attaches to estimations of the treatment of abnormally situated testes unless we consider the internal as well as the external secretions of the organ; on the other hand, an evaluation of the anatomical result alone is of but limited importance.

Before discussing the material from patients, I shall briefly consider the technique employed in the examination of sperm, and explain how I have classified the fertility, based upon the results of sperm examinations.

Practically all the samples have been produced by masturbation, usually in direct connexion with the objective examination, and after a period of abstinence that has only in a few cases been less than three days. Thus almost all the samples were examined in a state of absolute freshness.

The examinations comprised measurement of the amount of sperm, estimation of the percentage of motile spermatozoa, and evaluation of the motility and viability of the spermatozoa; further, an enumeration of spermatozoa per c.c. and—finally and most important—a differential count of smears stained with hæmatoxylin-eosin.

When we attempt to classify fertility according to the results obtained by sperm examination, it is of course impossible to draw distinct lines between various degrees for we must suppose that there is a gradual transition from the highest degree to a total arrest of fertility, that is, sterility. Yet the extremes are well known, because figures within normal limits must be presumed to mean normal fertility, while total absence of spermatozoa means sterility in all cases.

Between these extremes—normal fertility and sterility—I have made three grades, “presumably slight impairment of fertility”, “presumably moderate impairment of fertility” and “presumably severe impairment of fertility”. In classifying cases in the various categories I have considered all the results in detail of the sperm examination. The following classification is used at the University Institute of Forensic Medicine in Copenhagen.

*Slight impairment of fertility* is applied to cases showing (1) abnormal heads 21% to 30%, or (2) number of spermatozoa per c.c. 15 to 40 millions, or (3) amount of ejaculate 1 to 1.5 c.c.

*Moderate impairment of fertility* was presumed in the cases showing (1) abnormal heads 31% to 40%, or (2) number of spermatozoa per c.c. 5 to 15 millions, or (3) amount of ejaculate 0.5 to 1 c.c.

*Severe impairment of fertility* has been applied to cases showing (1) abnormal heads above 40%, or (2) number of spermatozoa per c.c. below 5 millions, or (3) amount of ejaculate less than 0.5 c.c.

The term *sterility* has only been applied to cases of aspermia, that is, cases in which no spermatozoa were found in the ejaculate.

I have divided the patients examined into four groups, A, B, C and D.

*Group A* comprises 11 patients with untreated bilateral cryptorchidism, that is, with their testes either situated in the abdomen or in the inguinal canal.



Group C comprises 43 patients with unilateral cryptorchidism treated with orchidopexy. These patients, too, had previously had a follow-up examination by Bjerre; there has been no selection of cases and the proportion of good, unsatisfactory and bad anatomical results is nearly the same as in Bjerre's original series.

Employing the same criteria as mentioned above, I have estimated the anatomical results of the operation. In these cases, where a normal, untreated testis is available for comparison, it is easier to detect even small deviations from normal; among these 43 testes only 3 were found in which no difference whatsoever could be demonstrated, whereas of course many cases were seen with a result that was extremely satisfactory from a purely anatomical point of view.

From 36 patients semen was obtained for examination. An estimation of the results regarding fertility is seen in fig. 2.

It appears that the fertility of the great majority of cases must be presumed to be normal or slightly reduced, while only a few displayed signs of a more serious reduction of fertility.

In 2 of the 3 patients with aspermia I succeeded in obtaining a biopsy from the normally situated testis, and in both cases normal spermiogenetic tissue was found. One of the patients was a sailor, but he did not think he had had any kind of venereal disease; the other patient had suffered from gonorrhoea ten years before the examination. So in both cases the aspermia was due to an occlusion of the efferent testicular ducts.

Group D comprises cases of unilateral cryptorchidism; namely, 30 patients with untreated cryptorchidism, in whom the retained testis is situated either in the abdomen or high up in the inguinal canal; and 12 patients in whom the retained testis had either been removed or transferred to an intraperitoneal position by operation. This gives a total of 42 patients who only possess one testis that is, and has always been, situated in its normal place in the scrotum. Thus, an examination of semen from these patients will reveal the nature of the sperm production in men who have only one testis which is able to function.

Sperm examinations have been made in 35 of the patients. The results in regard to fertility are shown in fig. 3.

It will be seen that normal conditions or a slight reduction of fertility are found in the great majority of cases; only a few display signs of considerable reduction.

In the patient who had aspermia the normally descended testis was a little smaller and of a definitely softer consistency than normal. I may mention that in still another patient in whom the testis was of soft consistency the sperm examination revealed signs of a severe reduction of fertility.

As I have stated, my purpose in examining these patients was to obtain material for comparison with the group that had been treated with orchidopexy for unilateral cryptorchidism.

As we have already seen, there is no difference between the two groups regarding the final result of the sperm examination—that is to say, in fertility; because in both groups the majority of patients must be labelled normal, or as showing signs of slight impairment of fertility. These designations were given to 25 cases in Group C (the operated patients), and to 24 cases in Group D (the patients who had not been operated on); only 8 and 10 cases respectively have been classified as having a moderate or severe impairment of fertility.

The other parts of the sperm examinations revealed practically identical conditions in the two Groups, but I will not go further into this, except as regards the question of the amount of spermatozoa.

By counting the number of spermatozoa we can obtain information about the concentration of spermatozoa in the ejaculate—that is, the number of spermatozoa per c.c.; but if the amount of the ejaculate is known we can also learn the total number of spermatozoa in the ejaculate, in other words we can get a *quantitative* measure of the entire sperm production of the testes.

As the two Groups C and D differ from one another in only one respect, namely that patients of the first group have one normal testis plus one testis treated by orchidopexy while patients of the second group—D—possess only one testis, we might suppose that a possible function of the operated testes would be revealed in a greater number of spermatozoa in these patients (Group C).

As I considered it important to have normal material for comparison, and was not able myself to procure it, I have taken some data published in 1938 by Hotchkiss, Brunner, and Grenley, using the part of their material derived from examinations of sperm samples produced by masturbation of 100 fertile men, thus taking it for granted that it will represent the values found in men with two normally situated testes.

In all my estimations of the anatomical results I have paid attention to all three factors, that is, size, consistency, and position. Judged from this point of view only 11 of the 52 testes, that is 21%, showed a result deserving to be called anatomically normal, while in the others I could detect great or small deviations from the normal regarding one or more of the conditions mentioned.

If, then, we examine the correlation between the anatomical results and the conclusions of the sperm investigations, we find that aspermia existed in the cases where all three factors—size, consistency, and position—differed from normal in both testes; also, as we should expect, in the cases where the testes had retracted to the inguinal canal or its immediate surroundings.

In the cases where normal conditions existed regarding all the three factors in at least one testis, this fact has—with one exception—been combined with the occurrence of spermatozoa in the ejaculate of the patient in question. On the other hand it is not possible to prove any correlation between the anatomical state of the testis and the *degree* of fertility, because an examination of sperm from these patients shows normal conditions as well as signs of all degrees of a reduced fertility.

It seems that softness of the testes indicates severe injuries, this condition having only been found once coinciding with spermatozoa in the ejaculate, while softness of the testes as the chief deviation from normal was combined with aspermia in 4 cases.

Summing up these results, we find that aspermia—that is, sterility—has been demonstrated in most cases of operatively treated bilateral cryptorchidism and that signs can be found of a more or less marked reduction of fertility in the cases where spermatozoa are produced by the operated testes.

These findings form a striking contrast to the mostly satisfactory results of other investigators, who usually report about 60% of good results. But these figures only apply to the anatomical outcome, whereas the functional result as regards spermatozoa production is considerably worse.

Besides having examined patients with bilateral cryptorchidism I have made an examination of two series of patients with unilateral cryptorchidism: (1) patients whose defect has been treated with orchidopexy, and (2) patients with untreated, still existing, unilateral cryptorchidism.

My purpose in examining these patients was this: if the operation had succeeded in making the operated testis produce significant amounts of spermatozoa, this must appear as a difference between the number of spermatozoa in the treated and untreated patients, for a greater number of spermatozoa would be found in the treated patients than in those not treated, seeing that the former ought to possess two sperm-producing testes, whereas the latter had only one. I have called these two series C and D, respectively.

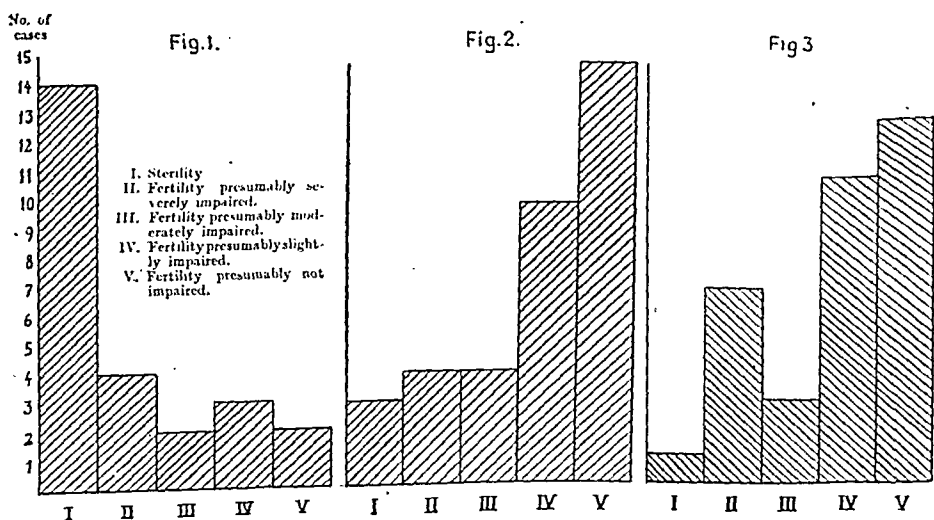


FIG. 1.—Results of the fertility estimates in Group B (patients treated with orchidopexy for bilateral cryptorchidism).

FIG. 2.—In Group C (patients treated with orchidopexy for unilateral cryptorchidism).

FIG. 3.—In Group D (patients with untreated unilateral cryptorchidism).

Their sperm material comes from patients with two testes, whereas mine comes from men with only one testis; we may therefore infer that the reason for the difference in our results is that men with two testes produce on an average twice as many spermatozoa as men with only one testis.

Thus the examinations of patients treated with unilateral orchidopexy point in the same direction as the investigations of patients with bilateral cryptorchidism, namely that by means of the operation we usually do not succeed in making the operated testis produce any significant amount of spermatozoa.

Moreover, these examinations of men with unilateral cryptorchidism reveal that the normally descended testis must be considered as capable of function as either of the two testes in normal men.

If we attempt to draw any conclusions regarding the treatment of cryptorchidism, based upon the investigations discussed here, I would say that we must regard the operative treatment with a good deal of pessimism, if the operation aims at making the retained testes produce spermatozoa, whereas it cannot be questioned that the operation offers relief in the various complications of cryptorchidism, first and foremost of the pain that may accompany the retention of the testis.

Considering first the *unilateral retention of the testis*, my investigations prove that fertility is identical in the treated and untreated patients, so that in this respect there has been no detectable effect of the operation. As on the whole the fertility of these patients must be considered normal, we must look upon unilateral cryptorchidism as an abnormality that does not in itself ask for any treatment, though of course pain, for instance, may supply an indication for operative treatment.

In the case of *bilateral retention of the testes* it is a much more serious question which treatment ought to be advised, because we must bear in mind that if the defect persists after the patient has passed puberty, he is sterile, and it will then be impossible for us with our present means to ameliorate his condition and render him fertile.

As previously emphasized, the results of operative treatment are very poor in regard to fertility.

I have no doubt that the only chance of fertility for these patients depends on the possibility that the testes will make a spontaneous descent to the scrotum before puberty is reached. We have learned from many investigations that at least half of the retained testes descend spontaneously in childhood, and that in certain forms of cryptorchidism, namely those where the testis is situated low in the inguinal region, descent occurs in almost 100% of cases; thus an operation performed on such cases can only do harm. I think, therefore, that in bilateral retention of the testes we should wait as long as possible for a spontaneous descent before resorting to operative treatment. If the descent has not taken place when puberty approaches, a hormonal treatment should be instituted in an attempt to provoke or accelerate the descent. It is very hard to state whether by hormonal treatment we obtain a descent of testes that would not have descended spontaneously, but if a hormonal treatment can accelerate the descent, at least something has been gained. If no descent has occurred on either side when puberty is approaching, operative treatment might be tried in order to attempt to ameliorate the miserable condition of bilateral cryptorchidism with its consequent sterility, but as regards fertility we must be ready for disappointment.

A bilateral orchidopexy should never be performed in one operation because of the risk of bilateral atrophy of the testes; when considering operative treatment we must bear in mind that some testes atrophy completely after operation—the number usually given is about 10% of cases. Even when a considerable space of time elapses between the two operations for bilateral retention we cannot feel quite safe about atrophy.

Another problem I will touch upon is the question of the condition which Mr. Denis Browne has named "superficial inguinal ectopic position", a condition in which the testis is situated in a "superficial inguinal pouch" above the external ring on the outside of the external oblique muscle. In Denmark we usually call this "inversio testis". Personally I have but little experience of it but I think that I can say that if this condition can be diagnosed with certainty—and only in that case—we might have a field here for operative treatment, but here again I think that we should be extremely cautious regarding the fertility prognosis.

In Denmark some surgeons have gone in for what they call "orchidolysis", merely loosening the testis without making any attempt to fix it in the bottom of the scrotum. Only the future can prove whether cases treated in this way have a better prognosis—and I should like to emphasize that only a follow-up examination of patients which includes sperm investigations will enable us to pronounce finally on the results of treatment of testicular retention.

#### REFERENCES

- HOTCHKISS, R. S., BRUNNER, E. K., and GRENLEY, P. (1938) *Amer. J. med. Sci.*, 196, 362.  
MACCOLLUM, D. W. (1935) *Arch. Surg.*, 31, 290.

Fig. 4 shows the curves of the number of spermatozoa per c.c. from my Groups C and D, and from the normal material of Hotchkiss and collaborators.

It will be seen that the curves for my groups are almost identical, and both have a similar shape to the curve for the normal material.

If we examine the curves of fig. 5, which shows the total number of spermatozoa in my two groups and in Hotchkiss's, you will observe that here also the curves are nearly identical and of the same shape as the curve for the normal material. A further characteristic of these curves is the fact that the peaks of both my curves are placed more to the left, that is, toward smaller values than those of the normal material.

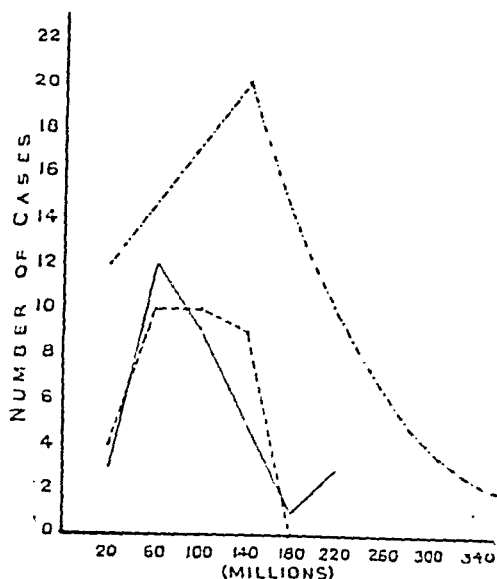


FIG. 4.—Curves of the spermatozoa count per c.c. from Groups C (—) and D (---), and after Hotchkiss *et al.* (1938) (-·-·-).

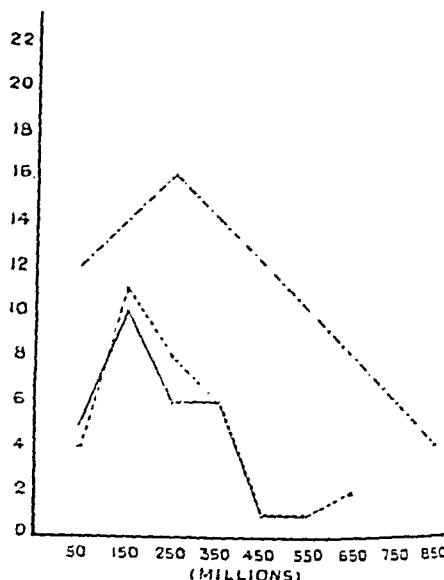


FIG. 5.—Curves of the total spermatozoa count in Groups C (—) and D (---), and after Hotchkiss *et al.* (1938) (-·-·-).

If we look at the same relations expressed in schematic form (Table I), we find the same

|                            | Spermatozoa count per c.c.<br>(in millions) |         |         | Total spermatozoa count<br>(in millions) |         |         |
|----------------------------|---------------------------------------------|---------|---------|------------------------------------------|---------|---------|
|                            | Lowest                                      | Highest | Average | Lowest                                   | Highest | Average |
| C .. ..                    | 4.4                                         | 214.7   | 77.8    | 10.1                                     | 974.2   | 232.4   |
| D .. ..                    | 0.5                                         | 139.7   | 63.1    | 2.0                                      | 611.1   | 186.1   |
| Hotchkiss <i>et al.</i> .. | 4.7                                         | 466.0   | 137.54  | 2.82                                     | 2330.0  | 429.68  |

characteristics as in the curves, namely that the average values for the Groups C and D are almost identical; and if we compare these average values with the corresponding values for the normal material, it will be seen that the latter are very nearly twice as great as the figures for my groups.

I am of opinion that the similarity proved between my Groups C and D must be due to the fact that the operative treatment of the patients in Group C has not succeeded in making the originally retained testis produce a number of spermatozoa sufficient to have any detectable influence on the average values; furthermore that on the whole these patients only produce spermatozoa with the normally descended testis, and that therefore they present the same conditions as the patients in Group D, in whom we can take it for granted that only the normally descended testis is capable of spermatozoa production.

As the same method in counting the spermatozoa has been employed by Hotchkiss and his collaborators, and as this method is easy and excludes any subjective judgment, I think we are justified in accepting as a fact that the difference between our material is that the number of spermatozoa in my cases is half as great as in theirs.

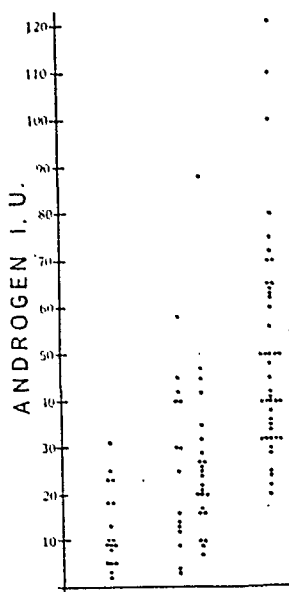


FIG. 1.—Androgen excretion in 24-hour urine samples. Column 1: Castrated men. Column 2: Cryptorchid men (operatively treated). Column 3: Cryptorchid men (not treated). Column 4: Normal men.

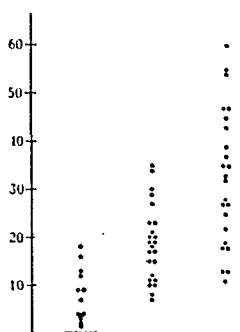


FIG. 2.—Androgen excretion in 24-hour urine samples. Figures on ordinate indicate the percentage growth of the test capons' combs. Column 1: Castrated adult male rabbits. Column 2: Experimentally cryptorchid adult male rabbits. Column 3: Normal adult male rabbits.

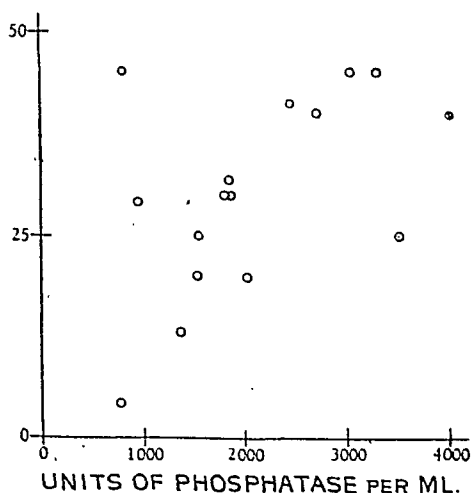


FIG. 3.—Correlation found between androgen excretion in a 24-hour urine sample and acid phosphatase in a semen specimen from bilateral cryptorchid men. (From H. Engberg, E. Andersson, B. Sury and J. Raft: The possibility of determining androgen production by measuring the acid phosphatase in semen: investigations in cryptorchid patients, *J. Endocr.*, 1947, 5, 44.)

Fig. 3 demonstrates the correlation found in cryptorchid men between the androgen excretion in the urine and the amount of acid semen phosphatase. By statistical analysis the correlation is found to be significant. In the cryptorchid men (16 persons) the average amount of phosphatase per millilitre is found to be 2,061 units. In normal men (173 persons) the average amount of 3,767 units was found. This means a reduction of acid phosphatase equivalent to the reduction of androgen excreted by cryptorchid men as compared to normal men. A similar reduction of androgen content in retained testes was found by Hanes and Hooker. When the experiments of Korenchevsky (1930) and Nelson (1937) are taken into consideration we may be justified in stating that retained testes produce less androgenic hormones than normal ones.

## Investigations on the Endocrine Function of the Testicle in Cryptorchidism

By HARALD ENGBERG, M.D., *Copenhagen.*

FOR centuries cryptorchidism has been known to impair the fertility of the individual. It was, however, unknown whether the testis preserved a normal endocrine function in cases of spontaneous retention in man. Judging solely from clinical observations retained testes seem to preserve their internal secretions to a great extent. Previous studies of experimental cryptorchidism have revealed that this condition reduces the production of androgenic hormone, and this in turn results in increased pituitary activity. Nothing definite is known about the production of oestrogen in cases of testicular retention.

The object of my investigations has been the hormone output in the urine of cryptorchid individuals. Determinations of the daily excretions of androgenic, oestrogenic and gonadotrophic hormones in the urine of cryptorchid men and boys have been carried out. Comparisons have been made with groups of normal and castrated persons. Altogether 200 persons have been examined. Similar determinations have been made in the urine and blood of experimentally cryptorchid animals, especially rabbits.

The conclusive part of my investigations may be summarized briefly as follows:

Fig. 1 demonstrates the excretion of androgenic hormone in the urine of 101 adult men during twenty-four hours. The numbers on the vertical axis mark the amounts of androgen in a twenty-four hour urine sample as measured by use of the capon's comb as test object. The amounts are given in international units since a comparison has been made with the international standard preparation of androsterone. The small black dots mark the single observations. The row most to the left indicates adult castrated men (18 persons). The average excretion is 11 i.u. More to the right you will find the men suffering from bilateral cryptorchidism; they are divided in two groups: 15 operated cases and 24 unoperated cases of bilateral cryptorchidism, average 25 and 26 i.u. respectively. Farthest to the right the dots record 44 normal men—average excretion 50 i.u. Quite an extensive statistical analysis of the data has been carried out, and I am justified in stating that the amount of androgen excreted in the urine by the bilateral cryptorchid men is significantly lower than in normal men but higher than in castrates.

I have examined a limited number of untreated bilateral cryptorchid boys—10 to 13 years of age. The androgen excretion for a twenty-four-hour period was compared with the excretion of a similar group of normal boys of the same age. The average amounts excreted were found to be almost equivalent. This is in accordance with the fact that the testes of cryptorchid boys at this age are microscopically identical to normal testes, though they may be slightly smaller.

Fig. 2 is similar to the first figure and shows the amount of androgen excreted in a twenty-four-hour urine sample of adult male rabbits. The numbers on the vertical axis mark the percentage of growth in the test-capon's comb during the test period. The groups are the same as in the previous figure: to the left the castrated animals, in the middle the experimentally cryptorchid rabbits and to the right the normal male rabbits. It will be seen directly that there is a distinct parallelism with the previously mentioned results.

TABLE I.—AVERAGE ANDROGEN EXCRETION IN A 24-HOUR URINE SAMPLE MEASURED IN INTERNATIONAL UNITS OR IN PERCENTAGE GROWTH OF THE TEST CAPON'S COMB.

|                       | Normal  | Cryptorchid | Castrated |
|-----------------------|---------|-------------|-----------|
| <i>Androgen:</i>      |         |             |           |
| Men .. .. .           | 50 i.u. | 26 i.u.     | 11 i.u.   |
| Boys .. .. .          | 4 i.u.  | 3 i.u.      | —         |
| Adult Male Rabbits .. | 33%     | 19%         | 4%        |

Hanes and Hooker (1937) extracted the androgenic hormone from the testes of normal and cryptorchid pigs. The testicles of the cryptorchid animals contained about 50% of the amount of androgen found in the normal testes, per weight unit.

In 1939 Gutman, in experiments with monkeys, found the amount of phosphatase in semen to be dependent on the amount of androgenic hormone present in the organism. The discovery by Gutman suggested that if a correlation could be established between the amount of androgen in the urine and the phosphatase in the semen of cryptorchid men, the androgen excretion in the urine might be taken as an expression of the androgen production of the organism.

In favour of the endocrine treatment are the results of some investigations on experimental cryptorchidism in rats in which I have participated. 177 rats were made cryptorchid on the right side only, by closing the inguinal canal by a silk purse-string suture after reposition of the testis in the abdominal cavity. 86 were treated by chorionic gonadotrophic hormone and 91 were kept as controls. Litter mates were used. It was found that large amounts of hormone did no harm to the testicles—neither the normal nor the undescended ones. We made another observation which we found later to be a confirmation of a statement by Moore. In the 91 controls the experimentally retained testis pushed its way through the abdominal wall into a newly formed inguinal pouch, or, more seldom, into the scrotum, in 8% of the cases. In the 86 cases which were treated by hormone a similar descent occurred in 22% of the cases. This seems to me to be a strong contradiction to the statement by Eisenstaedt *et al.* (1940), that chorionic gonadotrophic hormones will harm the retained testes which cannot be brought down by hormones. Rea (1941) has confirmed our evidence.

The highly purified commercial gonadotrophins extracted from the urine of pregnant women are well suited to the treatment of cryptorchidism. I have found no untoward reaction in administering such hormone to newborn babies in amounts of 1,000 i.u. per injection.

I believe—though I cannot substantiate my belief at present—that the hormonal treatment may be undertaken at a very early date. I am convinced that operative treatment of infantile hernias which are accompanied by undescended testes should not be resorted to before an attempt has been made to bring about descent by hormonal treatment. Even when descent has taken place operative treatment of infantile inguinal hernias is a very dubious affair and much harm may be done—especially by freeing a hernial sac as a whole from the cord in cases where it would have been sufficient to free the neck of the sac and cut it, with or without closure.

As retention of the testicle will need surgical intervention in a considerable number of cases, it must be borne in mind that there are few organs so liable to damage.

#### BIBLIOGRAPHY

- BERTELSEN, A., ENGBERG, H., and SAND, K. (1943) *Endokrinologie*, 25, 201.  
 BROWNE, DENIS (1938) *Brit. med. J.* (ii), 168.  
 BÜDINGER, K. (1923) *Med. Klinik*, 19, 893.  
 EISENSTAEDT, J. S., APPEL, M., and FRAENKEL, M. (1940) *J. Amer. med. Ass.*, 115, 200.  
 ENGBERG, H. (1948). The Endocrine Function of the Testicle in Cryptorchidism, M. D. Thesis. Copenhagen.  
 —, ANDERSSON, E., SURY, B., and RAFT, J. (1947) *J. Endocr.*, 5, 42.  
 GUTMAN, A. B., and GUTMAN, E. B. (1939) *Proc. Soc. exp. Biol. N.Y.*, 41, 277.  
 HAMBURGER, C., HALVORSEN, K., and PEDERSEN, J. (1945) *Acta Pharm. Tox.*, 1, 129.  
 HANES, F. M., and HOOKER, C. W. (1937) *Proc. Soc. exp. Biol.*, 35, 549.  
 HANSEN, T. S. (1946) *Acta chir. scand.*, 94, 117.  
 KORENCHESKY, V. (1930) *J. Path. Bact.*, 33, 607.  
 NELSON, W. O. (1937) *Cold Spring Harbor Symp. Quant. Biol.*, 5, 123.  
 REA, C. E. (1939) *Arch. Surg.*, 38, 1054.  
 — (1941) *Endocrinology*, 29, 288.  
 SAND, K., BERTELSEN, A., and ENGBERG, H. (1943) *Endokrinologie*, 25, 183.  
 WILSON, D. S. P. (1939) *Proc. R. Soc. Med.*, 32, 969.

Dr. P. M. F. Bishop: I am glad to see that we are all agreed upon one thing, that surgery by no means invariably produces successful functional results. This is at least an advance on the attitude of surgical optimism which used to exist in some quarters. I remember demonstrating a series of cases of undescended testicle treated by endocrine therapy at Guy's, and asking a distinguished surgical colleague who had kindly consented to attend the demonstration if he had any comment to make. He replied that he could see no need for endocrine therapy as in his experience surgical treatment was 100% successful. This can surely only be explained by supposing that he did not follow up his cases.

Mr. Browne states that no one has contradicted his views on the surgical anatomy of the undescended testicle. There are, however, a number of descriptions which do not conform to Mr. Browne's hypothesis, though this is perhaps not the place to engage in a detailed anatomical argument. I would therefore refer him only to one observer, McGregor (1929), whose theory of the "third inguinal ring", does not agree with the theory advanced by Mr. Browne.

Our disagreement appears to be on the subject of the percentage of canalicular testes one encounters. It is considerably higher in my opinion than he has suggested, and it is these canalicular testes which present such a difficult problem to the surgeon, because the cord is too short to allow the testis to be placed in the scrotum without tension on the blood-vessels.

The output of oestrogenic and gonadotrophic hormones in the urine of adult bilateral cryptorchid men—as compared to normal and castrated men—may be summarized in Table II.

TABLE II.

|                       |    |    |    | Adult men |             |           |
|-----------------------|----|----|----|-----------|-------------|-----------|
|                       |    |    |    | Normal    | Cryptorchid | Castrated |
| <i>Oestrogen:</i>     |    |    |    |           |             |           |
| > 20 m.u. . .         | .. | .. | .. | 14        | 20          | 1         |
| < 20 m.u. . .         | .. | .. | .. | 0         | 2           | 15        |
| <i>Gonadotrophin:</i> |    |    |    |           |             |           |
| < 17 r.u. . .         | .. | .. | .. | 21        | 7           | 3         |
| > 17 r.u. . .         | .. | .. | .. | 2         | 16          | 13        |

The determination of oestrogenic hormone in a twenty-four-hour urine sample has been made in a semi-quantitative manner (*see* Hamburger, *et al.*, 1945). For the sake of convenience the results have been classified in two groups, having more or less than 20 mouse units. It will be seen from the table that excretion of less than 20 m.u. in twenty-four hours does not occur in normal men. But all the castrated men except one excreted less than 20 m.u. Among all the bilateral cryptorchid men only 2 had an output of less than 20 m.u.

The determination of the excretion of gonadotrophic hormones has also been carried out by a semi-quantitative method. According to Hamburger (1945) an excretion of more than 17 rat units (equivalent to 50 mouse units) is very seldom found in normal men. In the group of 23 normal men here included only 2 had an output of more than 17 r.u. in a twenty-four-hour sample. It may be mentioned that the same two persons were found to excrete 24 i.u. of androgen in the same sample, which amount is at the lower limit of the normal androgen excretion. 80% of the castrates had an output of more than 17 rat units, and so had 70% of the untreated bilateral cryptorchid men.

This confirms the findings of Nelson in experimental cryptorchidism: the increased pituitary activity is a result of the decreased androgen production.

As to the androgen excretion of the bilateral cryptorchid men in whom orchidopexy had been previously performed, the average amount excreted in twenty-four hours is 26 i.u. as compared to the 25 i.u. in the unoperated group. In 50% of the operated men the gonadotrophic hormone excretion was increased and the oestrogen excretion lowered.

My investigations have been published at a moment when the more pessimistic say that any treatment of cryptorchidism is useless. Denis Browne has pointed out that hormone treatment will not bring down any testis which would not have descended without it though it may hurry the descent. Ample support to this statement was given by Wilson (1939) and by Rea (1941). Operative treatment, especially orchidopexy, has been criticized severely. Rea is well aware of its disadvantages but still finds orchidopexy a justifiable procedure. Dr. T. S. Hansen has not been able to find much support for this belief. My investigations give no evidence in favour of orchidopexy. On this background it is not very encouraging to call attention to the fact that cryptorchidism not only seriously hampers the fertility of the individual but has a very noxious influence on the endocrine function of the retained testis.

Confronted with the belief that a retained testis is best treated by being left alone, I should like to point out why this cannot be done.

The majority of all cases of true cryptorchidism suffer from complications such as hernia, pain or both. Operative treatment must be undertaken in a great number of cases for these reasons. If orchidopexy is not a justifiable procedure some other form of operation must take its place.

Hormone treatment cannot be discarded, either. According to Denis Browne the most important single point in the diagnosis of testicular position is the distinction between the superficial inguinal ectopia and the so-called high-retractile position which is a normal variation. The high-retractile testis descends spontaneously or after hormone treatment. The superficial inguinal ectopic testis does not—operation alone may bring it down. Büdinger (1923) and later authors stress the fact that inguinal ectopia constitutes one-third of all cases diagnosed as retention of the testicle. Two-thirds of all cases rightly or wrongly classified as testicular retention in boys show spontaneous descent. Most of these cases are "high-retractile" testes which respond well to treatment by hormones.

In order to distinguish the cases of superficial inguinal ectopia—needing operation before the testis is seriously damaged—from the cases of high-retractile testes—which very likely will be hurt by operation—hormone treatment is a very valuable adjunct, and may be the key to an early diagnosis. Denis Browne believes that if a testis is seen through the skin in the inguinal region it is ectopic. If not visible the diagnosis may be difficult.



The endocrine treatment are the results of some investigations on experimental in rats in which I have participated. 177 rats were made cryptorchid on the by closing the inguinal canal by a silk purse-string suture after reposition of abdominal cavity. 86 were treated by chorionic gonadotrophic hormone pt as controls. Litter mates were used. It was found that large amounts of harm to the testicles—neither the normal nor the undescended ones. We observation which we found later to be a confirmation of a statement by 91 controls the experimentally retained testis pushed its way through the into a newly formed inguinal pouch, or, more seldom, into the scrotum, in . In the 86 cases which were treated by hormone a similar descent occurred in . This seems to me to be a strong contradiction to the statement by Eisenstaedt at chorionic gonadotrophic hormones will harm the retained testes which ght down by hormones. Rea (1941) has confirmed our evidence.

urified commercial gonadotrophins extracted from the urine of pregnant l suited to the treatment of cryptorchidism. I have found no untoward inistering such hormone to newborn babies in amounts of 1,000 i.u. per

ugh I cannot substantiate my belief at present—that the hormonal treatment en at a very early date. I am convinced that operative treatment of infantile re accompanied by undescended testes should not be resorted to before an a made to bring about descent by hormonal treatment. Even when descent operative treatment of infantile inguinal hernias is a very dubious affair may be done—especially by freeing a hernial sac as a whole from the cord t would have been sufficient to free the neck of the sac and cut it, with or

of the testicle will need surgical intervention in a considerable number of , borne in mind that there are few organs so liable to damage.

#### BIBLIOGRAPHY

- ENGBERG, H., and SAND, K. (1943) *Endokrinologie*, 25, 201.  
 (1938) *Brit. med. J.* (ii), 168.  
 (1923) *Med. Klinik*, 19, 893.  
 S., APPEL, M., and FRAENKEL, M. (1940) *J. Amer. med. Ass.*, 115, 200.  
 948). The Endocrine Function of the Testicle in Cryptorchidism, M. D. Thesis.  
 SSSON, E., SURY, B., and RAFT, J. (1947) *J. Endocr.*, 5, 42.  
 and GUTMAN, E. B. (1939) *Proc. Soc. exp. Biol. N.Y.*, 41, 277.  
 , HALVORSEN, K., and PEDERSEN, J. (1945) *Acta Pharm. Tox.*, 1, 129.  
 and HOOKER, C. W. (1937) *Proc. Soc. exp. Biol.*, 35, 549.  
 (1946) *Acta chir. scand.*, 94, 117.  
 V. (1930) *J. Path. Bact.*, 33, 607.  
 (1937) *Cold Spring Harbor Symp. Quant. Biol.*, 5, 123.  
 ) *Arch. Surg.*, 38, 1054.  
*Endocrinology*, 29, 288.  
 ELSSEN, A., and ENGBERG, H. (1943) *Endokrinologie*, 25, 183.  
 (1939) *Proc. R. Soc. Med.*, 32, 969.

ishop: I am glad to see that we are all agreed upon one thing, that surgery riarily produces successful functional results. This is at least an advance of surgical optimism which used to exist in some quarters. I remember series of cases of undescended testicle treated by endocrine therapy at g a distinguished surgical colleague who had kindly consented to attend the he had any comment to make. He replied that he could see no need for y as in his experience surgical treatment was 100% successful. This can lained by supposing that he did not follow up his cases.

ates that no one has contradicted his views on the surgical anatomy of the ele. There are, however, a number of descriptions which do not conform hypothesis, though this is perhaps not the place to engage in a detailed ent. I would therefore refer him only to one observer, McGregor (1929), he "third inguinal ring", does not agree with the theory advanced by Mr.

nt appears to be on the subject of the percentage of canalicular testes one considerably higher in my opinion than he has suggested, and it is these which present such a difficult problem to the surgeon, because the cord is the testis to be placed in the scrotum without tension on the blood-vessels.

The output of oestrogenic and gonadotrophic hormones in the urine of adult bilateral cryptorchid men—as compared to normal and castrated men—may be summarized in Table II.

TABLE II.

|                       |    |    |    | Adult men |             |           |
|-----------------------|----|----|----|-----------|-------------|-----------|
|                       |    |    |    | Normal    | Cryptorchid | Castrated |
| <i>Oestrogen:</i>     |    |    |    |           |             |           |
| > 20 m.u. . .         | .. | .. | .. | 14        | 20          | 1         |
| < 20 m.u. . .         | .. | .. | .. | 0         | 2           | 15        |
| <i>Gonadotrophin:</i> |    |    |    |           |             |           |
| < 17 r.u. . .         | .. | .. | .. | 21        | 7           | 3         |
| > 17 r.u. . .         | .. | .. | .. | 2         | 16          | 13        |

The determination of oestrogenic hormone in a twenty-four-hour urine sample has been made in a semi-quantitative manner (*see* Hamburger, *et al.*, 1945). For the sake of convenience the results have been classified in two groups, having more or less than 20 mouse units. It will be seen from the table that excretion of less than 20 m.u. in twenty-four hours does not occur in normal men. But all the castrated men except one excreted less than 20 m.u. Among all the bilateral cryptorchid men only 2 had an output of less than 20 m.u.

The determination of the excretion of gonadotrophic hormones has also been carried out by a semi-quantitative method. According to Hamburger (1945) an excretion of more than 17 rat units (equivalent to 50 mouse units) is very seldom found in normal men. In the group of 23 normal men here included only 2 had an output of more than 17 r.u. in a twenty-four-hour sample. It may be mentioned that the same two persons were found to excrete 24 i.u. of androgen in the same sample, which amount is at the lower limit of the normal androgen excretion. 80% of the castrates had an output of more than 17 rat units, and so had 70% of the untreated bilateral cryptorchid men.

This confirms the findings of Nelson in experimental cryptorchidism: the increased pituitary activity is a result of the decreased androgen production.

As to the androgen excretion of the bilateral cryptorchid men in whom orchidopexy had been previously performed, the average amount excreted in twenty-four hours is 26 i.u. as compared to the 25 i.u. in the unoperated group. In 50% of the operated men the gonadotrophic hormone excretion was increased and the oestrogen excretion lowered.

My investigations have been published at a moment when the more pessimistic say that any treatment of cryptorchidism is useless. Denis Browne has pointed out that hormone treatment will not bring down any testis which would not have descended without it though it may hurry the descent. Ample support to this statement was given by Wilson (1939) and by Rea (1941). Operative treatment, especially orchidopexy, has been criticized severely. Rea is well aware of its disadvantages but still finds orchidopexy a justifiable procedure. Dr. T. S. Hansen has not been able to find much support for this belief. My investigations give no evidence in favour of orchidopexy. On this background it is not very encouraging to call attention to the fact that cryptorchidism not only seriously hampers the fertility of the individual but has a very noxious influence on the endocrine function of the retained testis.

Confronted with the belief that a retained testis is best treated by being left alone, I should like to point out why this cannot be done.

The majority of all cases of true cryptorchidism suffer from complications such as hernia, pain or both. Operative treatment must be undertaken in a great number of cases for these reasons. If orchidopexy is not a justifiable procedure some other form of operation must take its place.

Hormone treatment cannot be discarded, either. According to Denis Browne the most important single point in the diagnosis of testicular position is the distinction between the superficial inguinal ectopia and the so-called high-retractile position which is a normal variation. The high-retractile testis descends spontaneously or after hormone treatment. The superficial inguinal ectopic testis does not—operation alone may bring it down. Büdinger (1923) and later authors stress the fact that inguinal ectopia constitutes one-third of all cases diagnosed as retention of the testicle. Two-thirds of all cases rightly or wrongly classified as testicular retention in boys show spontaneous descent. Most of these cases are "high-retractile" testes which respond well to treatment by hormones.

In order to distinguish the cases of superficial inguinal ectopia—needing operation before the testis is seriously damaged—from the cases of high-retractile testes—which very likely will be hurt by operation—hormone treatment is a very valuable adjunct, and may be the key to an early diagnosis. Denis Browne believes that if a testis is seen through the skin in the inguinal region it is ectopic. If not visible the diagnosis may be difficult.

In favour of the endocrine treatment are the results of some investigations on experimental cryptorchidism in rats in which I have participated. 177 rats were made cryptorchid on the right side only, by closing the inguinal canal by a silk purse-string suture after reposition of the testis in the abdominal cavity. 86 were treated by chorionic gonadotrophic hormone and 91 were kept as controls. Litter mates were used. It was found that large amounts of hormone did no harm to the testicles—neither the normal nor the undescended ones. We made another observation which we found later to be a confirmation of a statement by Moore. In the 91 controls the experimentally retained testis pushed its way through the abdominal wall into a newly formed inguinal pouch, or, more seldom, into the scrotum, in 8% of the cases. In the 86 cases which were treated by hormone a similar descent occurred in 22% of the cases. This seems to me to be a strong contradiction to the statement by Eisenstaedt *et al.* (1940), that chorionic gonadotrophic hormones will harm the retained testes which cannot be brought down by hormones. Rea (1941) has confirmed our evidence.

The highly purified commercial gonadotrophins extracted from the urine of pregnant women are well suited to the treatment of cryptorchidism. I have found no untoward reaction in administering such hormone to newborn babies in amounts of 1,000 i.u. per injection.

I believe—though I cannot substantiate my belief at present—that the hormonal treatment may be undertaken at a very early date. I am convinced that operative treatment of infantile hernias which are accompanied by undescended testes should not be resorted to before an attempt has been made to bring about descent by hormonal treatment. Even when descent has taken place operative treatment of infantile inguinal hernias is a very dubious affair and much harm may be done—especially by freeing a hernial sac as a whole from the cord in cases where it would have been sufficient to free the neck of the sac and cut it, with or without closure.

As retention of the testicle will need surgical intervention in a considerable number of cases, it must be borne in mind that there are few organs so liable to damage.

#### BIBLIOGRAPHY

- BERTELSEN, A., ENGBERG, H., and SAND, K. (1943) *Endokrinologie*, 25, 201.  
 BROWNE, DENIS (1938) *Brit. med. J.* (ii), 168.  
 BÜDINGER, K. (1923) *Med. Klinik*, 19, 893.  
 EISENSTAEDT, J. S., APPEL, M., and FRAENKEL, M. (1940) *J. Amer. med. Ass.*, 115, 200.  
 ENGBERG, H. (1948). The Endocrine Function of the Testicle in Cryptorchidism, M. D. Thesis. Copenhagen.  
 —, ANDERSSON, E., SURY, B., and RAFT, J. (1947) *J. Endocr.*, 5, 42.  
 GUTMAN, A. B., and GUTMAN, E. B. (1939) *Proc. Soc. exp. Biol. N.Y.*, 41, 277.  
 HAMBURGER, C., HALVORSEN, K., and PEDERSEN, J. (1945) *Acta Pharm. Tox.*, 1, 129.  
 HANES, F. M., and HOOKER, C. W. (1937) *Proc. Soc. exp. Biol.*, 35, 549.  
 HANSEN, T. S. (1946) *Acta chir. scand.*, 94, 117.  
 KORENCHESKY, V. (1930) *J. Path. Bact.*, 33, 607.  
 NELSON, W. O. (1937) *Cold Spring Harbor Symp. Quant. Biol.*, 5, 123.  
 REA, C. E. (1939) *Arch. Surg.*, 38, 1054.  
 — (1941) *Endocrinology*, 29, 288.  
 SAND, K., BERTELSEN, A., and ENGBERG, H. (1943) *Endokrinologie*, 25, 183.  
 WILSON, D. S. P. (1939) *Proc. R. Soc. Med.*, 32, 969.

**Dr. P. M. F. Bishop:** I am glad to see that we are all agreed upon one thing, that surgery by no means invariably produces successful functional results. This is at least an advance on the attitude of surgical optimism which used to exist in some quarters. I remember demonstrating a series of cases of undescended testicle treated by endocrine therapy at Guy's, and asking a distinguished surgical colleague who had kindly consented to attend the demonstration if he had any comment to make. He replied that he could see no need for endocrine therapy as in his experience surgical treatment was 100% successful. This can surely only be explained by supposing that he did not follow up his cases.

Mr. Browne states that no one has contradicted his views on the surgical anatomy of the undescended testicle. There are, however, a number of descriptions which do not conform to Mr. Browne's hypothesis, though this is perhaps not the place to engage in a detailed anatomical argument. I would therefore refer him only to one observer, McGregor (1929), whose theory of the "third inguinal ring", does not agree with the theory advanced by Mr. Browne.

Our disagreement appears to be on the subject of the percentage of canalicular testes one encounters. It is considerably higher in my opinion than he has suggested, and it is these canalicular testes which present such a difficult problem to the surgeon, because the cord is too short to allow the testis to be placed in the scrotum without tension on the blood-vessels.

But it is because the cord is short, owing to inadequate "luteinizing hormone" stimulation, that these cases often respond well to endocrine therapy. Whether this treatment merely "accelerates" a descent which would occur spontaneously at a later date is irrelevant, for though many of these testicles will descend spontaneously at the age of 15 or 16, by this time the seminiferous tubules may well be irrevocably atrophied, according to the careful histological observations of Cooper (1929). It would seem, therefore, important to ensure that the testicle is in the scrotum at the latest by the twelfth birthday.

As to the dangers and disadvantages of endocrine therapy, Mr. Browne does not need to remind the members of this particular Section that endocrine preparations may be powerful and potent substances. Enlargement of the penis will certainly occur with overdosage or too prolonged administration. It is as well to see the patient at the end of a two-months course, and seldom to prolong treatment for more than six months. Mr. Browne has been unfortunate in his experience of the prevalence of undesirable psychological disturbances following endocrine therapy. A fairly extensive perusal of the literature (Bishop, 1945) left me surprised at the rarity with which such complications occur.

I believe that endocrine therapy is of value in suitably selected cases, but I feel that the best results will be obtained by an intimate and careful collaboration between the surgeon and the endocrinologist.

#### REFERENCES

- BISHOP, P. M. F. (1945) *Guy's Hosp. Rep.*, 94, 12.  
 COOPER, E. R. A. (1929) *J. Anat.*, 64, 5.  
 MCGREGOR, A. L. (1929) *Surg. Gynec. Obstet.*, 49, 273.

Mr. L. R. Broster showed illustrations of a series of testes collected at Charing Cross Hospital, and reported on by Professor Vines. The patients included intersexes, cryptorchids with hypospadias, and varying grades of undescended. In some cases the patients had erroneously been brought up as females.

In bilateral ectopia, the histology generally corresponds to that of the hermaphrodite pig, where the tubules are atrophic and the interstitial cells hyperplastic, and suggests that this condition may be of endocrine origin, although spermatogenesis may occur. In unilateral undescended on the other hand, there is progressive fibrosis after puberty, there is atrophy of the tubules, and the interstitial cells are absent.



FIG. 1.—Bilateral ectopia, "female", aged 16. Complete atrophy of the tubules with an islet of hyperplastic interstitial tissue (high magnif.).



FIG. 2.—Bilateral ectopia, "female", aged 32. Active spermatogenesis is present; small groups of interstitial cells are present in normal numbers (high magnif.).



FIG. 3.—Bilateral ectopia, "female", aged 55. The field consists entirely of hyperplastic interstitial cells in which no tubules are seen (high magnif.).



FIG. 4.—Bilateral ectopia, male, aged 23. Dark masses of hyperplastic interstitial cells lie between the atrophic tubules (high magnif.).



FIG. 5.—Hermaphrodite bacon pig, aged 7 months. The tubules are atrophic and the interstitial cells hyperplastic (low magnif.).

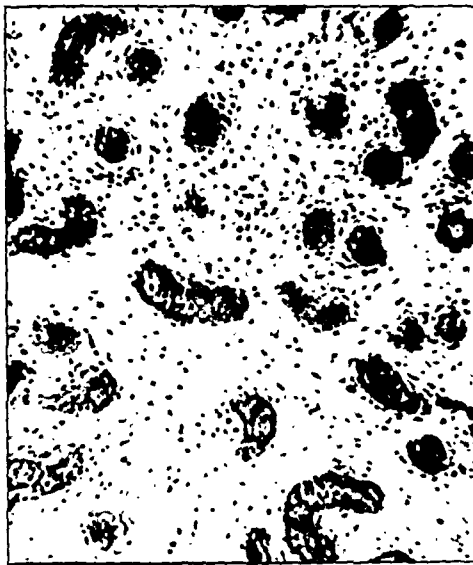


FIG. 6.—Unilateral ectopia, aged 10. Pre-pubertal group, showing the fetal and immature type of testis (low magnif.).

But it is because the cord is short, owing to inadequate] "luteinizing hormone" stimulation, that these cases often respond well to endocrine therapy. Whether this treatment merely "accelerates" a descent which would occur spontaneously at a later date is irrelevant, for though many of these testicles will descend spontaneously at the age of 15 or 16, by this time the seminiferous tubules may well be irrevocably atrophied, according to the careful histological observations of Cooper (1929). It would seem, therefore, important to ensure that the testicle is in the scrotum at the latest by the twelfth birthday.

As to the dangers and disadvantages of endocrine therapy, Mr. Browne does not need to remind the members of this particular Section that endocrine preparations may be powerful and potent substances. Enlargement of the penis will certainly occur with overdosage or too prolonged administration. It is as well to see the patient at the end of a two-months course, and seldom to prolong treatment for more than six months. Mr. Browne has been unfortunate in his experience of the prevalence of undesirable psychological disturbances following endocrine therapy. A fairly extensive perusal of the literature (Bishop, 1945) left me surprised at the rarity with which such complications occur.

I believe that endocrine therapy is of value in suitably selected cases, but I feel that the best results will be obtained by an intimate and careful collaboration between the surgeon and the endocrinologist.

#### REFERENCES

- BISHOP, P. M. F. (1945) *Guy's Hosp. Rep.*, 94, 12.  
 COOPER, E. R. A. (1929) *J. Anat.*, 64, 5.  
 MCGREGOR, A. L. (1929) *Surg. Gynec. Obstet.*, 49, 273.

Mr. L. R. Broster showed illustrations of a series of testes collected at Charing Cross Hospital, and reported on by Professor Vines. The patients included intersexes, cryptorchids with hypospadias, and varying grades of undescended. In some cases the patients had erroneously been brought up as females.

In bilateral ectopia, the histology generally corresponds to that of the hermaphrodite pig, where the tubules are atrophic and the interstitial cells hyperplastic, and suggests that this condition may be of endocrine origin, although spermatogenesis may occur. In unilateral undescended on the other hand, there is progressive fibrosis after puberty, there is atrophy of the tubules, and the interstitial cells are absent.



FIG. 1.—Bilateral ectopia, "female", aged 16. Complete atrophy of the tubules with an islet of hyperplastic interstitial tissue (high magnif.).



FIG. 2.—Bilateral ectopia, "female", aged 32. Active spermatogenesis is present; small groups of interstitial cells are present in normal numbers (high magnif.).



FIG. 3.—Bilateral ectopia, "female", aged 55. The field consists entirely of hyperplastic interstitial cells in which no tubules are seen (high magnif.).



FIG. 4.—Bilateral ectopia, male, aged 23. Dark masses of hyperplastic interstitial cells lie between the atrophic tubules (high magnif.).



FIG. 5.—Hermaphrodite bacon pig, aged 7 months. The tubules are atrophic and the interstitial cells hyperplastic (low magnif.).



FIG. 6.—Unilateral ectopia, aged 10. Pre-pubertal group, showing the fetal and immature type of testis (low magnif.).

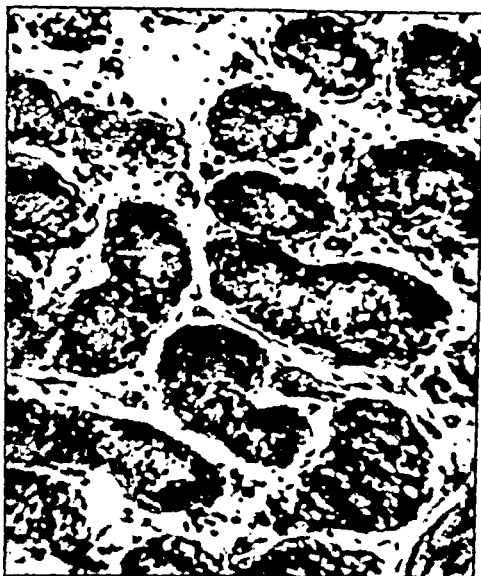


FIG. 7.—Unilateral ectopia, aged 12. Pubertal group, showing an attempt at spermatogenetic development (medium magnif.).



FIG. 8.—Unilateral ectopia, aged 16. Post-pubertal group. Atrophic changes are well marked and the interstitial cells are absent (medium magnif.).



FIG. 9.—Unilateral ectopia, aged 24. Post-pubertal group (medium magnif.).

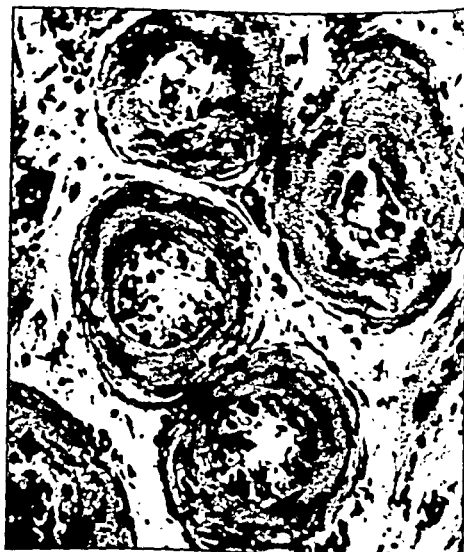


FIG. 10.—Unilateral ectopia, aged 66. Post-pubertal group, showing extreme atrophy of the tubules (medium magnif.).



## Section of Surgery

President—JULIAN TAYLOR, C.B.E., M.S., F.R.C.S.

[April 6, 1949]

### DISCUSSION ON RESECTABLE CARCINOMA OF THE STOMACH

**Professor John Morley :** It is, I think, a matter for serious discussion whether the trans-thoracic attack on carcinoma in the upper half of the stomach, which has so greatly extended the scope of surgery in this field, is better left to the thoracic surgeon, or whether the abdominal surgeon should accustom himself to this route. The ideal solution, that the two specialists should combine in these operations, is perhaps hardly feasible in most hospitals since the harvest is too great and the labourers few.

Whatever may be thought about this division of labour, we may agree that all surgeons who undertake transpleural gastrectomies should be well versed both in the technique of gastro-intestinal suture and in the after-care of the patient with a thoracotomy wound. That the anaesthetist should be an expert in thoracic work goes without saying.

There is in the profession a widespread feeling of pessimism as to the end-results of gastrectomy for cancer. This pessimism, as I hope to show, is not altogether justified, and it tends to hamper our efforts by leading to a most undesirable delay before the patient is brought to operation. Doctors who believe that cancer of the stomach means death within a year or two whatever we do will scarcely consider it an urgent matter to get the patient early to the surgeon. Harnett, in his statistical analysis of 1,405 cases of cancer of the stomach from various hospitals in the County of London (1947), found that 19% were treated symptomatically for over three months before they were referred to hospital. And we must remember that patients themselves often hesitate for several months after the onset of symptoms before consulting the doctor, while even after admission to hospital a strange delay sometimes occurs in the medical wards.

All these delays will inevitably lower the resectability rate and prejudice the end-results. Let us consider first the proportion of cases that are found to be resectable. Of Harnett's 1,405 cases from London, only 17.3% were resected. Harnett (1947) considers that 26% or roughly 1 case in 4 may be taken as the average resectability rate at present, and that agrees with my experience over the last thirty years, though there has been some improvement in later years. The Mayo Clinic figures (Walters *et al.*, 1948) are distinctly better than that, and in their last report they state that, in 1947, of 275 patients operated on, 148 or 53.8% had growths that were resected. These figures are hardly comparable with Harnett's or with mine since they do not take into consideration the patients who were inoperable on admission but only those that were actually operated on.

**Operative mortality.**—In my own series of 140 gastrectomies for cancer the mortality, 21.4%, is much too high, judged by present standards. My cases include those from many years back, before we realized the importance of such measures as pre-operative blood transfusion in anæmic patients, or of keeping up the blood volume after operation, and before penicillin and the sulpha drugs had robbed chest complications of their terror. I have always felt, in dealing with cancer, that where there is a remote chance of a radical cure, one should give the patient the benefit of surgery without too tender a regard for one's own statistics. But even in recent years, in a series of 152 gastrectomies for cancer in the Manchester Royal Infirmary from the years 1940–48 inclusive, the operative mortality was 19.7%. This compares very unfavourably with the latest figures from the Mayo Clinic, where 144 gastrectomies for cancer were done in 1947 with an operative mortality of only 9 or 6.3%—a truly remarkable achievement when we consider what poor material these patients are; though no doubt they reach the Mayo Clinic in better condition than the average hospital patient in this country.

TABLE I.—MANCHESTER ROYAL INFIRMARY

CASES OF CARCINOMA OF STOMACH 1940-1948

Total Number—622.

|                            |     |                 |
|----------------------------|-----|-----------------|
| Not treated .. ..          | 316 |                 |
| Radical operation .. ..    | 152 | Died 30 = 19.7% |
| Palliative operation .. .. | 154 |                 |

Survived radical operation—122.

|                                      |    |
|--------------------------------------|----|
| Died under three years .. ..         | 56 |
| Alive with recurrence .. ..          | 3  |
| Alive and well after six years .. .. | 6  |
| " " " " five " .. ..                 | 6  |
| " " " " four " .. ..                 | 4  |
| " " " " three " .. ..                | 3  |
| " " " " under three years .. ..      | 33 |

Later recurrence

|                                              |   |
|----------------------------------------------|---|
| Died under six years .. ..                   | 1 |
| " " five " .. ..                             | 4 |
| " " four " .. ..                             | 3 |
| Alive with recurrence under four years .. .. | 1 |
| Untraced .. ..                               | 2 |

Total 122

*The end-results.*—We have to accept the grim fact that of patients who survive the operation of gastrectomy for cancer, about half will die of a recurrence within two years. Out of 152 gastrectomies done in the Manchester Royal Infirmary from 1940-48, 122 survived the operation. Of these, 52 died within two years. This is rather less than half, but of the 1948 cases 18 are at present alive and well, and a large proportion of these may be expected to recur and die within the next two years.

One must urge in mitigation of this gloomy picture that a considerable proportion of these gastrectomies, a proportion not easy to ascertain precisely, should really be regarded as palliative measures. A subtotal gastrectomy is by far the best palliative operation for cancer when it is feasible, and even though early secondaries in the liver or peritoneum or in inaccessible lymph glands make it certain that the patient will not be cured, the operation is well worth doing for the completeness of the temporary relief and the longer postponement of the inevitable end, as compared with a mere gastro-enterostomy.

TABLE II.—PERSONAL SERIES

Total Number of Gastrectomies—140

|                                                                     |     |
|---------------------------------------------------------------------|-----|
| Died .. ..                                                          | 30  |
| Survived operation .. ..                                            | 110 |
| Died of recurrence within three years .. ..                         | 64  |
| Untraced .. ..                                                      | 18  |
| Died of coronary thrombosis after twenty-one and a half years .. .. | 1   |
| Alive and well after twenty-one years .. ..                         | 2   |
| " " " " twenty years .. ..                                          | 2   |
| " " " " eleven years .. ..                                          | 1   |
| " " " " eleven years (then untraced for thirteen years) .. ..       | 1   |
| " " " " eight years .. ..                                           | 1   |
| " " " " seven years .. ..                                           | 1   |
| " " " " six years .. ..                                             | 1   |
| " " " " five years .. ..                                            | 2   |
| " " " " four years .. ..                                            | 3   |
| " " " " three years .. ..                                           | 3   |
| " " " " under three years .. ..                                     | 5   |

Late recurrences

|                                              |   |
|----------------------------------------------|---|
| Died from recurrence after eight years .. .. | 1 |
| " " " " four years .. ..                     | 3 |
| " " " " three years .. ..                    | 1 |

Total 110

Although the vast majority of recurrences give a fatal result within three years there are a few cases of fairly late recurrence in my series. The latest death from recurrence was eight years after operation, 3 recurred and died in four years and 1 in three years. 18 patients are untraced, most of whom may be presumed to have died under three years.

The chief point that emerges from these figures is that the few patients who survive five years have a fair prospect of a permanent cure. In cancer of the stomach very late recurrence seems to be much more unusual than in cancer of the breast, where we see not uncommonly local recurrences ten, fifteen, twenty, or even twenty-five years after a radical mastectomy.

The complete series from the Manchester Royal Infirmary Register for a more limited period from 1940-1948 shows similar results (Table I).

Here again we see that about half the patients that survive operation die within three years, and that those who get over five years show little tendency to recur.

Earlier diagnosis is of supreme importance if surgery is to have a chance in this disease, and up to the present no other therapeutic measure but surgery holds out any hope.

Precious time might be saved if we could get the profession to believe that cancer of the stomach can be cured if we can only get the patients early enough.

In the earliest stage of gastric carcinoma our unaided clinical diagnosis can seldom amount to more than a shrewd suspicion. We are dependent on radiology for a precise diagnosis as a rule, fortified on occasion by the gastroscope.

*Hypertrophic stenosis of pylorus as a cause for error in diagnosis.*—I must mention here a condition which gives rise to an erroneous diagnosis of pyloric carcinoma, not commonly, but sufficiently often to make it important. I have records of 9 cases of hypertrophic pyloric stenosis in adults of cancer age, all of which were difficult or impossible to differentiate from early carcinoma on radiological evidence, or even on inspection and palpation when the stomach was exposed at operation.

The condition was first brought prominently before the profession in 1933 when Kirklin described 81 cases from the Mayo Clinic in the course of 60,000 gastric examinations, and it is noteworthy that only 1 of the 81 cases was diagnosed accurately by the radiologist; nearly all were regarded as pyloric neoplasm. My colleague, the late Dr. E. W. Twining, described 3 cases in 1933. Twining believed that the circular muscle of the pyloric canal only was hypertrophied, and not the actual pyloric sphincter. My own sections do not show this clear demarcation between pre-pyloric and pyloric musculature.

This condition may occur in association with a peptic ulcer, either gastric or duodenal, or may be found unassociated with any ulceration. Fig. 1 is a gastric radiograph and fig. 2 is



FIG. 1.—Radiograph showing pyloric filling defect in a case of hypertrophic stenosis of the pylorus in an adult.

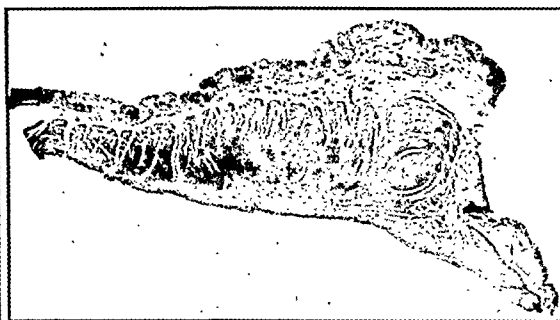


FIG. 2.—Section of hypertrophic pyloric stenosis (same case as fig. 1) showing hypertrophic circular muscle of pyloric canal and sphincter.

a section of the pylorus from a doctor aged 52, who was sent to me with a diagnosis of early carcinoma of the pylorus. At operation pyloric hypertrophy was so great that the pyloric canal felt very like an early cancer. Although I suspected that it was a simple muscular hypertrophy I felt that the only safe course was to treat it as a carcinoma, and I did a subtotal gastrectomy. No ulcer was present in this case, nor any extra-gastric cause of pyloric spasm that could be discovered. Another case was a man aged 61, with a long history of indigestion. The X-ray report was "Ulcer in the pyloric antrum which involves a good deal of stomach tissue and is therefore presumably malignant". Operation disclosed marked hypertrophy of the pyloric canal, simulating carcinoma, and a small chronic ulcer on the lesser curvature. A Schoemaker gastrectomy was done.

It should be realized that this condition may disappear spontaneously. A woman aged 44, who had a history of fifteen years' indigestion, had been examined radiologically by Dr.

E. D. Gray in 1934, when she had a typical X-ray appearance of hypertrophic pyloric stenosis. I operated on her nine years after and found a chronic ulcer of the lesser curvature, for which I did a Schoemaker gastrectomy, but she now had no hypertrophic pyloric stenosis.

*The technique of gastrectomy for cancer.*—I believe that some form of subtotal gastrectomy will remain the standard operation for pyloric and pre-pyloric carcinoma. My own preference is for the Schoemaker modification of the Billroth I operation described by me in 1928, because I can remove as much stomach by this method as by the Polya type of operation and it is less liable, as Bentley and I showed in 1938, to result in secondary anaemia. Some surgeons have suggested that total gastrectomy should often be preferred to the subtotal operation, even for pyloric neoplasms, but that would involve a greatly increased operative mortality without much prospect of a compensating increase in the late survival rate. For all cancers of the cardiac end or the upper half of the stomach the transthoracic operation is now the method of choice, and many of these gastrectomies will perforce be total, while some will involve in addition removal of the spleen, and the tail and body of the pancreas, and even the transverse colon. But the real hope of controlling this fell disease lies, not in ever more extensive operations but in diagnosing the condition so early that the subtotal gastrectomy will be effective. And we may cherish the hope that ultimately the biochemist will find a remedy that will make the surgeon's efforts in this field no longer necessary.

#### REFERENCES

- HARNETT, W. L. (1947) *Brit. J. Surg.*, 34, 379.  
 KIRKLIN, R. R. (1933) *Amer. J. Roentgenol.*, 39, 4.  
 MORLEY, J. (1928) *Brit. J. Surg.*, 16, 239.  
 —, and BENTLEY, F. H. (1938) *Brit. med. J.* (ii), 645.  
 TWINING, E. W. (1933) *Brit. J. Radiol.*, 6, 644.  
 WALTERS, W. GRAY, PRIESTLEY, J. T., and WAUGH, J. M. (1948) *Proc. Mayo Clin.*, 23, 554.

**Mr. Norman C. Tanner:** It is still unhappily the universal experience of surgeons engaged in the treatment of gastric carcinoma to find that the majority of cases, even of those who survive radical resection, die within five years. Nevertheless, radical resection of the tumour relieves pain, vomiting and anaemia, restores the patient to his home and usually to his work. Even a year of such relief fully repays the surgeon's efforts, and at the age at which gastric carcinoma usually appears, it is a most valuable addition to the patient's life. No one who compares the after-histories of the resected with those of the unresected cases of gastric carcinoma can doubt the great happiness and relief conferred even by palliative surgery, particularly if some hope of cure can be entertained.

What is the position of the patient treated to-day, only ten years after the cases analysed by Harnett were treated?

Operative mortalities have diminished in operations involving all parts of the stomach. Therefore, with a much higher number of resections and higher percentage of survivors of resection, I think we can look forward to a definite increase in the number of cases of gastric carcinoma who will live five years or more.

The greatest operative advances have taken place in resection of growths involving the upper stomach and so I propose to confine my remarks to a few points concerning the technique of upper gastric resection.

*The approach.*—Although total gastrectomy by the abdominal route has been successfully carried out for many years, there is no doubt that, except in a few patients with lax viscera, it is often technically difficult because the final œsophageal anastomosis is made at a great distance, while the œsophagus is tense, and in addition a bulky tumour may intrude on the great line of vision. The result is often that the anastomosis is insecure and tends to leak, and the resection is restricted in extent. Furthermore, for truly radical resection it may be desirable to remove some of the lower œsophagus, and this is even more hazardous and often impossible by the abdominal route. The change to a transthoracic approach has made resection of a length of œsophagus easy and has made it possible to construct the anastomosis from a convenient distance and angle. As a result leakage from the suture line has become a rarity and in my transthoracic œsophageal anastomoses following resection of the lower œsophagus or upper stomach there has been no leakage. In addition, more liberal œsophageal resection has almost eliminated that unfortunate group where recurrence took place at the suture line.

Although Ohsawa recommended an abdomino-thoracic incision in 1933, most English and American surgeons for a time favoured a formal postero-lateral thoracotomy. I now feel no doubt, however, that for total gastrectomy or removal of the upper stomach an abdomino-thoracic approach is better.

*Abdomino-thoracic approach.*—The patient is laid on his right side and firmly fixed so.

It is an advantage to have a tilting table, so that during the early part of the operation there is a slight dorsal tilt, and toward the latter part a slight ventral tilt, while the anastomosis is being made. The abdominal part of the incision is transverse, commencing in the mid-line halfway between xiphisternum and umbilicus and extending laterally to the costal margin (fig. 1). This is deepened down through the peritoneum and through this incision the



FIG. 1.—Healed abdomino-thoracic incision.

gastric tumour and all parts of the peritoneal cavity may be palpated. If the tumour appears to be operable, then the incision is continued along the eighth intercostal space, as far back as the lateral edge of the erector spinæ muscle. It is convenient to identify this space with the palpating left hand in the abdomen. A little more room is given if a rib is resected. A part of the costal margin may be removed to prevent overriding when the wound is closed. The pleural cavity is best opened anteriorly in the costophrenic sulcus below the lung. The wound is spread open by means of an abdominal retractor placed in the abdominal part of the incision. The diaphragm is divided from its periphery to the œsophageal hiatus. This gives a perfect exposure from the duodenum to the lower œsophagus (figs. 2A and 2B). The

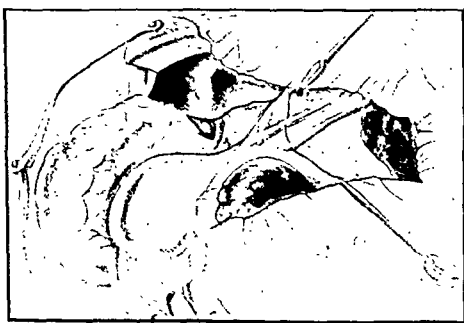


FIG. 2A.—Exposure through abdomino-thoracic incision. Œsophagus, spleen and whole stomach accessible.

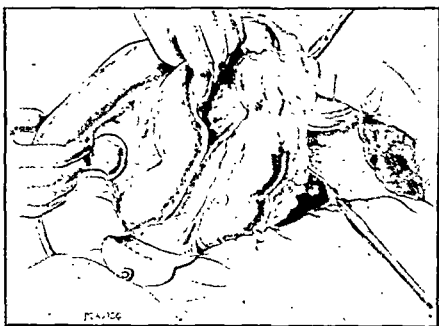


FIG. 2B.—Exposure through abdomino-thoracic incision. On lifting the colon the jejunum is readily accessible.

part which I used to find difficult through a purely thoracic incision, the closure of the duodenum, is made very easy. The small intestine is also very accessible.

*The anastomosis.*—It has become a routine practice after resection of the upper part of the stomach or œsophagus to close the cut end of the stomach, and anastomose the divided end of the œsophagus into an incision in the anterior wall of the stomach. It has been considered risky to make an end-to-end œsophago-gastric anastomosis. I have, however, used end-to-end anastomoses exclusively for three years, both for upper partial gastrectomy when the œsophagus and stomach were anastomosed and for total gastrectomy when œsophagus and jejunum were anastomosed. This method has the advantage of greater simplicity in technique, and it enables one to make the anastomosis with less tension, or, alternatively, to resect more stomach or œsophagus. In addition it functions excellently and in

every case in which I have passed an œsophagoscope post-operatively I have found it possible to introduce the instrument into the stomach or jejunum with ease.

The exact technique of anastomosis varies, according to the amount of stomach removed. If most of the stomach is removed, a triangular part of the pyloric antrum is left (fig. 3). In such a case I close part of each end of the cut surface and anastomose the œsophagus to the middle part. The two angles left are then brought against the side of the œsophagus and sutured to it, thus greatly strengthening the anastomosis (figs. 4 and 5).

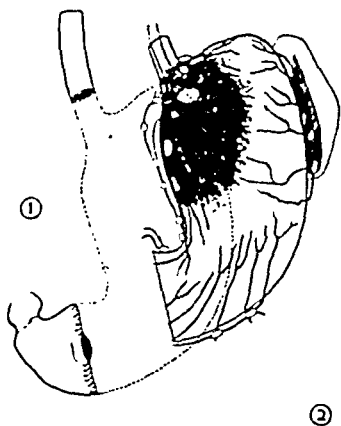


FIG. 3.

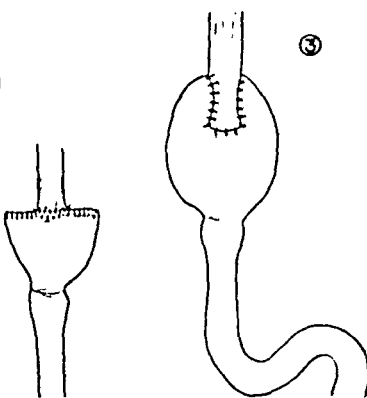


FIG. 4.



FIG. 5.

FIG. 3.—If most of the stomach is removed a triangular part of the pyloric antrum is left, stage (1), and the œsophagus is anastomosed end-to-end to its middle part, stage (2).

FIG. 4.—The two angles left are sutured against the side of the œsophagus, stage (3).

FIG. 5.—X-ray after end-to-end anastomosis of œsophagus to pyloric antrum.

If much of the stomach is conserved, as is permissible in the case of tumours very localized to the cardia (though the glands around the left gastric artery must always be removed), then an oblique cut end results (fig. 6). Much of the lesser curve side and a minimum of the greater curve side is closed and again an end-to-end anastomosis is made. The lesser curve side is then inverted, the greater curve end is stitched against the side of the œsophagus to diminish tension and reinforce the suture line (fig. 7). If possible a third row of sutures is used to give added safety. Fig. 8 is an X-ray photograph after this type of anastomosis.

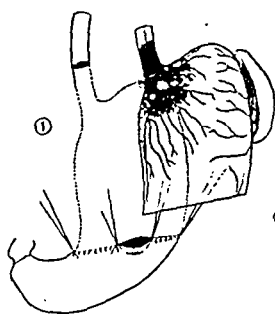


FIG. 6.

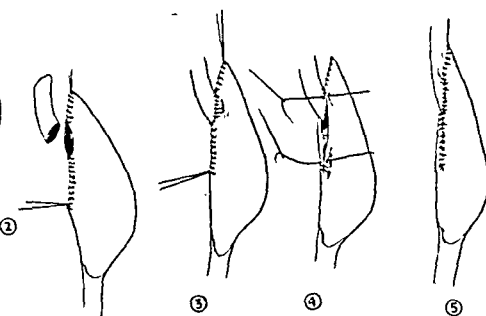


FIG. 7.



FIG. 8.

FIG. 6.—The body of the stomach is transected leaving an oblique cut end, stage (1), and the œsophagus is anastomosed end-to-end near but not at the greater curvature, stage (2).

FIG. 7.—The short projecting part of the greater curve is sutured against the side of the œsophagus and the lesser curve side is inverted, stages (3), (4) and (5).

FIG. 8.—X-ray after end-to-end anastomosis of œsophagus to body of stomach.

In the more extensive upper gastric neoplasms it is necessary to remove the whole stomach. In such cases I transect the jejunum and mobilize it after the method of Roux, and make an end-to-end œsophago-jejunostomy (fig. 9). This undoubtedly leaves the safest and most comfortable reconstruction possible after total gastrectomy (fig. 10).

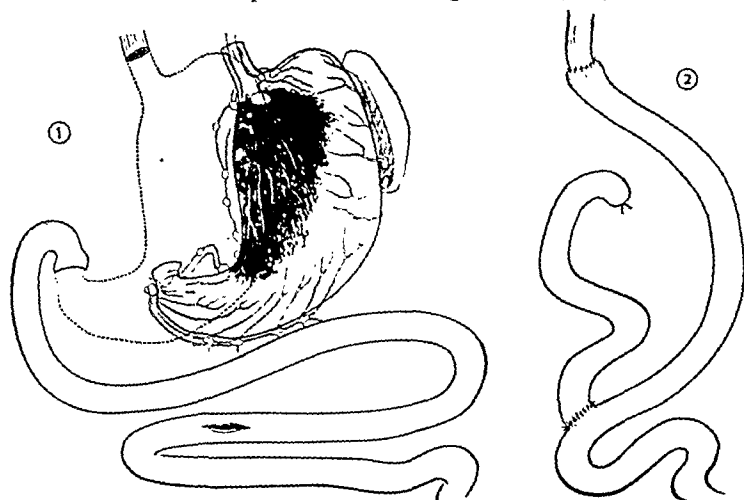


FIG. 9.—Total gastrectomy, stage (1), with end-to-end œsophago-jejunostomy, stage (2).



FIG. 10.—End-to-end œsophago-jejunostomy. A pocket of air tends to collect in the dilated jejunum.

In all these anastomoses the part anastomosed to the œsophagus is drawn well up and then anchored with interrupted fine silk sutures to the mediastinal pleura, to obviate tension. I think it is most important, however, not to stitch the pleura too snugly and so close off the mediastinum completely, or a closed mediastinal infection may become possible. The mediastinum must be left free to drain into the pleural cavity. Any pleural exudate can subsequently be removed by aspiration for I have found it more convenient to aspirate post-operative pleural exudates than to leave in a pleural drain.

*The limits of resectability of gastric carcinoma.*—There has been of late years a great widening of the limits of resectability of gastric tumours. Upward and downward exten-

sions to the œsophagus and duodenum demand only a little more dissection for their extirpation. Extension of upper gastric carcinoma into the diaphragm can be dealt with by the excision of a ring of diaphragm round the œsophageal hiatus. Extension into the left lobe of the liver may, in the absence of distant metastases, be treated by the removal of part or the whole of the left lobe.

The great omentum should be removed as a routine because the gastro-epiploic glands are often to be found some distance below the gastro-epiploic arch and may otherwise be left behind. The lesser omentum tends to be invaded at an early stage and should be removed flush with the liver.

Extension of the growth through the posterior wall of the stomach, either into the pancreas or into the peritoneum of the posterior wall of the lesser sac, lends itself particularly well to radical removal. In such cases, instead of dividing the gastro-splenic omentum, an incision is made in the peritoneum lateral to the spleen and upper stomach, and the spleen, pancreas, and peritoneum of the lesser sac are all reflected forward and to the right, exposing adrenal and perinephric tissue until the coeliac axis is found (fig. 11). Here the splenic and left gastric arteries and veins are tied and the pancreas is transected well to the right. In this way all the peritoneum of the lesser sac except that investing colon and mesocolon may be removed (fig. 12). An added advantage of this resection, as pointed out by Allison (1946) three years

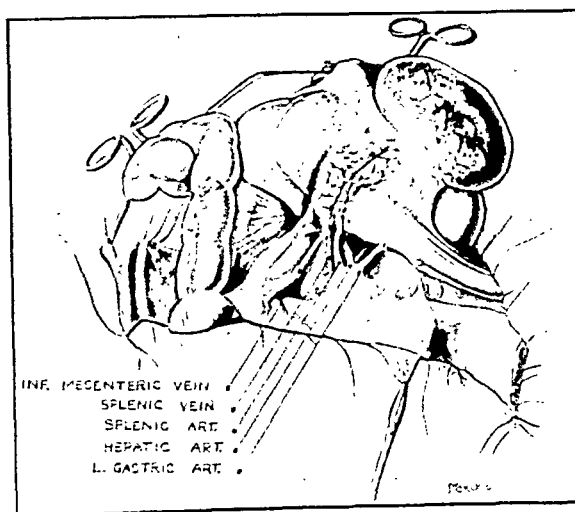


FIG. 11.

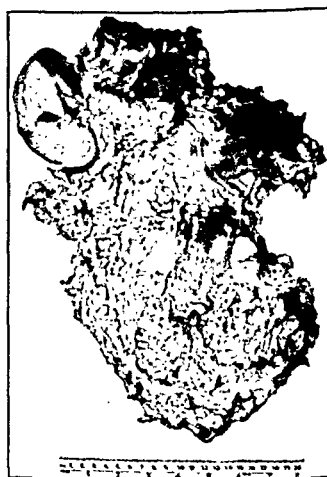


FIG. 12.

FIG. 11.—The spleen, stomach and pancreas are reflected to the right together with the posterior wall of the lesser sac.

FIG. 12.—Posterior view of specimen after pancreatico-gastrectomy illustrating that most of the posterior wall of the lesser sac is in the specimen (obscuring the posterior wall of the stomach).

ago, is that the middle and left suprapancreatic glands, which drain much of the stomach, are also removed. It does not add much in time to the operation, in fact it is time-saving on occasions. I have usually been able to complete the procedure within three hours, often less. In occasional cases even the mesocolon or colon should be resected if either is invaded by growth.

Incidentally, in such cases there is usually no colonic obstruction, so I would recommend resection and immediate anastomosis rather than a Mikulicz type of repair, for after such massive resections there is a shift of all the viscera to fill the empty left hypochondrium and if a colostomy is present it is placed under great tension.

What is the state and prognosis of the patient who has survived such massive resections, and are these justifiable?

Pack and McNeer (1948) found that in cases where an adjacent organ was removed with a carcinoma of the stomach, the prognosis was improved. No doubt the type of tumour which is advanced enough to invade an adjacent organ before distant or peritoneal metastases have appeared must be a localizing type of tumour so that complete local removal gives a better prognosis than is normally to be expected.

After these massive resections the patients remain in good general condition, eat well and



can return to work. After total gastrectomy combined with subtotal pancreatectomy there may be, at first, some looseness of the bowel, but this soon subsides and the patient finally has only one or two slightly relaxed motions a day. At a late stage the nutrition may be excellent, and post-cibal discomfort absent.

## BIBLIOGRAPHY

- ALLISON, P. R. (1946) *Proc. R. Soc. Med.*, 39, 411.  
 PACK, G. T., and MCNEER, G. (1948) *Surgery*, 24, 769.

**Professor F. A. R. Stammers:** In taking part in this discussion, I make no claim to long experience in gastric surgery but rather that I am like many others who, returning from the Services, and having experienced the recent numerous advances, find themselves with a reasonable number of beds and associated with medical colleagues inviting them to undertake gastric work.

**Introduction.**—We have all experienced the quickening progress and experience of war regarding such matters as readily available blood; better understanding of fluid, chloride and protein balance—how to recognize and rectify imbalance; the sulphonamides and penicillin; confidence in use of the thoraco-abdominal route to the upper left abdomen, engendered by experience in treating thoraco-abdominal wounds as also subsequently by watching one's thoracic colleagues making their new attack on the lower œsophagus, thereby making the thorax one of the broad highways of surgery; and, finally, the great advances in anæsthetics whereby it is possible to have chest and abdomen wide open for one and a half to two hours with complete safety—much credit is due to our anæsthetic colleagues. All this, together with the work of such authorities as Churchill, Phemister, Lahey, Wangenstein, Allison and others, turned one's thoughts to the idea of a bolder attack on gastric cancer.

**Statistics.**—The figures from different Centres concerning cancer of the stomach are most constant. In Birmingham our Cancer Follow-up Department, under the direction of Miss Levi, has attained the remarkable achievement of tracing 99% of the 1,486 cases attending the Birmingham Teaching Hospitals between 1936 and 1947.

TABLE I.—CARCINOMA OF STOMACH—BIRMINGHAM 1936–1947

| Year        | Totals | No treatment | Laparotomy only | Palliative operation only | Some type gastrectomy | Survivals (years) |    |    |    |    |    |    |
|-------------|--------|--------------|-----------------|---------------------------|-----------------------|-------------------|----|----|----|----|----|----|
|             |        |              |                 |                           |                       | 1                 | 2  | 3  | 4  | 5  | 7  | 10 |
| 1936        | 83     | 46           | 16              | 13                        | 8                     | 10%               | 3% | 1% | 1% | 1% | 1% | 0  |
| 1937        | 72     | 35           | 19              | 8                         | 10                    | 16%               | 5% | 4% | 1% | 0  | 0  | 0  |
| 1938        | 140    | 79           | 28              | 12                        | 21                    | 19%               | 6% | 4% | 4% | 3% | 2% | 1% |
| 1939        | 138    | 66           | 35              | 20                        | 17                    | 18%               | 8% | 6% | 4% | 4% | 3% | 0  |
| 1940        | 120    | 64           | 30              | 12                        | 14                    | 15%               | 7% | 5% | 3% | 3% | 3% | 0  |
| 1941        | 128    | 61           | 26              | 17                        | 24                    | 16%               | 7% | 4% | 2% | 2% | 0  | 0  |
| 1942        | 105    | 58           | 22              | 6                         | 19                    | 16%               | 7% | 3% | 1% | 1% | 0  | —  |
| 1943        | 130    | 57           | 46              | 11                        | 16                    | 14%               | 7% | 3% | 2% | 1% | 0  | —  |
| 1944        | 107    | 55           | 23              | 13                        | 16                    | 13%               | 7% | 4% | 4% | —  | —  | —  |
| 1945        | 148    | 76           | 37              | 11                        | 24                    | 13%               | 6% | 5% | —  | —  | —  | —  |
| 1946        | 151    | 64           | 39              | 15                        | 33                    | 14%               | 7% | —  | —  | —  | —  | —  |
| 1947        | 164    | 90           | 32              | 13                        | 29                    | 14%               | —  | —  | —  | —  | —  | —  |
| Grand total | 1,486  | 751          | 353             | 151                       | 231                   |                   |    |    |    |    |    |    |

Of these 1,486 cases, only 24 survived more than three years, only 14 more than five years. It is of interest and may not be without significance that these longest survivors were all treated by no more than partial gastrectomy; and Finsterer (1945) stated that his 50 longest survivors were also treated by partial gastrectomy only.

In studying *post-mortem findings* one finds that death usually results from liver secondaries or generalized metastasis, but in a minority there is recurrence of growth in the stump of the stomach, and a few of these latter might have been saved by subtotal or total gastrectomy. Undoubtedly, however, the main hope of improvement in results still lies in earlier diagnosis.

**Available operations.**—The available procedures which attempt to eradicate malignant disease of the stomach are:

- |                          |                                                                                              |
|--------------------------|----------------------------------------------------------------------------------------------|
| (1) Partial gastrectomy. | } Combined, according to operative findings, with splenectomy and/or partial pancreatectomy. |
| (2) Subtotal gastrectomy |                                                                                              |
| (3) Total gastrectomy    |                                                                                              |

Subtotal and total gastrectomy may be performed by either the abdominal route or the

abdomino-thoracic route. By "subtotal" we mean that the section passes through the oesophageal mucous membrane on the lesser curve side, but leaves a 4-5 centimetre rim of fundus on the greater curvature, whereas Finsterer's definition of "subtotal gastrectomy" is to preserve about 10 cm. of fundus. We feel that the distinction is important, since our technique more nearly approaches the pathological advantages of the "total" procedure, yet, as will be recounted, it is free from some of the early post-operative complications associated with complete removal of the stomach.

Figs. 1 and 2 show the post-mortem specimen of the only death amongst the 12 subtotal

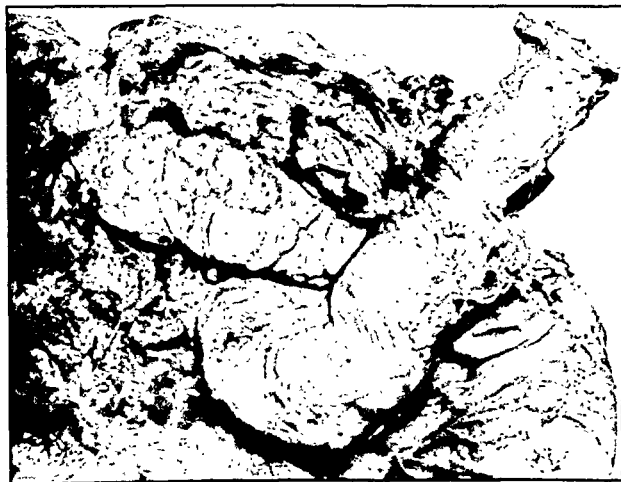


FIG. 1.

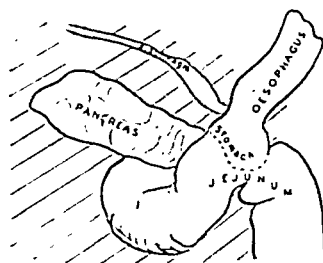


FIG. 2.

FIGS. 1 and 2.—Specimen from only death following subtotal gastrectomy, showing extent of ablation.

gastrectomies to be described, and figs. 3 and 4 the post-operative barium meal radiographs in typical subtotal and total gastrectomy cases respectively.

*Present series.*—In Birmingham a group of us, consisting of A. L. d'Abreu, B. N. Brooke, D. M. Morrissey, R. H. F. Brain and myself, have been combining our experiences in the problem of gastric cancer. There are 12 cases of "subtotal" gastrectomies (as defined above) with one operative death, and 7 cases of total gastrectomies with 2 operative deaths. For so lethal a condition as cancer of the stomach such an operative mortality is justifiable, although results should improve with further experience.

*Choice of case.*—The general constitutional health of the patient should be reasonably good, and his age be under 65 years.

*Preparation.*—Pre-operative investigation and preparation are of the greatest importance and any abnormality in haemoglobin, blood chlorides or plasma proteins must be rectified, this being especially important where vomiting has been prominent. Since there seems definite evidence of deficiency in vitamins B and C, we also believe that pre-operative exhibition of nicotinic acid, riboflavine and ascorbic acid is useful.

*Operation.*—The principles of the more radical procedures have already been dealt with by Mr. Tanner and are well described in the writings of Wangensteen and Lahey.

Believing with Wangensteen and Lahey that total gastrectomy is often possible via the abdominal route, and also, from the experience of this small series, that the immediate post-operative complications of the subtotal operation are less than with total gastrectomy, we have adopted the oblique incision across the upper abdomen in line with the left eighth rib, as suggested by A. L. d'Abreu. The general exploration of growth, glandular involvement, liver and pelvis is carried out through the abdominal part of the wound. It affords remarkably good access to the left upper abdomen and, after mobilizing the left lobe of the liver in the Grey Turner manner, particularly to underneath the left cupola of the diaphragm and, therefore, to the oesophagus. In thickset patients or in those with a narrow costal angle or where the growth has involved the oesophagus, or so near to it as to mean that effective

access can only be obtained through the diaphragm, the chest is opened by extending the incision along the eighth rib. Where this proves necessary, it is important, where possible, that the diaphragm should be reconstituted and the œsophago-jejunostomy made in such a manner that the pinch-cock effect of the diaphragm be preserved, i.e. that the anastomosis be kept below the diaphragm. I also believe that where subtotal gastrectomy seems to be well clear of the growth, this should be the choice of operation, since immediate complications are minimized. Regarding the actual anastomosis, it is desirable to divert the pancreatic juices from the œsophagus by performing an entero-anastomosis when a loop of jejunum has been used, or to employ a Roux-en-Y type of junction. Once again it is emphasized that, with increasing experience, one succeeds in achieving these extensive ablations without recourse to opening the chest.

*Immediate post-operative care.*—With careful pre-operative preparation, with intravenous saline followed by blood during the operation, together with good anæsthesia, the condition of the patient at the end of these extensive procedures should, nevertheless, be good, the pulse being 80-90 and the systolic blood-pressure above 100 mm.Hg. No fluid is given by mouth during the first twelve hours, but the intravenous fluids are continued to about 5 pints per twenty-four hours, there being on an average 1 pint of normal saline, 1 of plasma and 3 pints of 5% glucose. The Ryle's tube, which, at operation, was guided into the afferent loop, is



FIG. 3.—Radiograph of barium meal in case of subtotal gastrectomy.



FIG. 4.—Radiograph of barium meal in case of total gastrectomy.

removed at the end of twelve hours. During the first three or four days careful watch is kept on the urine volume and chloride excretion *per diem*—these should be over 1,000 c.c. and 4 to 6 grammes respectively. Upon the latter finding is decided the amount of saline to be given intravenously. Fluids by mouth, one ounce hourly, are permitted from twelve hours onwards.

Hæmoglobin and plasma protein estimations are made on the fifth or sixth day, and usually require correction, either by whole blood or by the supernatant serum, present supplies of dried plasma conveying the risk of homologous serum jaundice. Hypoproteinæmia is also corrected by high protein diet of the Varco type, from the fifth day onwards.

When the chest has been opened, X-ray pictures are taken on alternate days to check the

presence of any effusion. The usual in-bed exercises are instituted from the beginning in order to prevent phlebothrombosis as also any tendency to chest complications.

#### EARLY POST-OPERATIVE COMPLICATIONS

*Regurgitation.*—We have found that total gastrectomies performed via the thoraco-abdominal route show a marked tendency to regurgitate, and that this is especially so when the œsophagus has been shortened and the diaphragm reconstituted below the anastomosis. It often leads to œsophagitis, stomatitis and glossitis, which makes swallowing so painful that one patient died of inanition rather than suffer the pain. Entero-anastomosis, or the employment of the Roux-en-Y single loop anastomosis, does much to prevent this regurgitation and there is no doubt that it is less common when the chest has not been opened and the diaphragm not incised. On the contrary, it is remarkable how rare is regurgitation when a small 3–4 cm. rim of fundus is preserved, as we do in subtotal gastrectomy. I suspect that many surgeons would regard this all-but-total ablation as indeed a total gastrectomy, but unless the operative specimen consists of duodenal mucous membrane at one end and œsophageal mucous membrane at the other, one is not entitled to call it "total". So striking is this freedom that one is forced to believe that this very small residuum of stomach acts as a reservoir—on the X-ray picture it looks about the size of a golf ball (fig. 3).

*Glossitis.*—Following total gastrectomy we have had several patients who, about the eighth to tenth day, have developed blisters on the tongue, breaking down into ulcers (fig. 5).

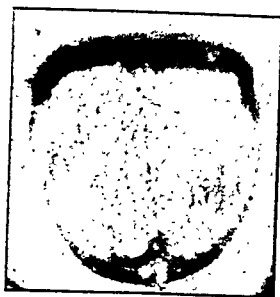


FIG. 5.—Example of glossitis about ten days after total gastrectomy.



FIG. 6.—Same case two weeks later, treated by nicotinic acid and riboflavine.

The tongue is very sore, and this is aggravated by drinking. There has usually been regurgitation, though not always of a severe degree, and the most striking feature is, as Brain has pointed out, that the condition responds to the exhibition of nicotinic acid and riboflavine. In one case, the patient developed an ichthyotic rash reminiscent of vitamin-B deficiency, and this also promptly cleared up with vitamin treatment. The glossitis probably results from a combination of vitamin B and C deficiencies and regurgitation.

#### LATE POST-OPERATIVE FEATURES

*Post-prandial fullness.*—This is almost to be expected, and must be mechanical. It tends to improve, and it is amazing how comparatively large meals can be taken.

*Failure to gain weight.*—This may be associated with inability to take as full meals as hitherto, but it may also be connected with a disturbance of fat absorption.

*Looseness of stools.*—This feature is almost universal and often is quite troublesome during the first few months. Brain has been investigating the problem, and it appears to be associated with steatorrhœa, fat absorption sometimes being as low as 45%. The stools are loose, pale and offensive. Factors to be considered are (a) some neurogenic involvement of the pancreas and/or bowel, affecting the secretory and motor functions respectively, and (b) alteration of the flora and fauna of the upper bowel. There is no evidence of associated failure of liver function.

*Anæmia.*—Secondary anæmia is not uncommon, and can be rectified by iron or blood transfusion. Macrocytic hyperchromic anæmia may develop after three or four years.

#### SUMMARY

Life is quality not quantity—are these operations worth while? I am satisfied that we must try them out, since with modern devices they are relatively safe and will become safer. The

post-operative comfort of the subtotal gastrectomies—perhaps one should call it “near-total”—is unquestioned. Where a total gastrectomy is essential one must anticipate certain discomforts, though with increasing experience these will probably be circumvented, and in any case they are less than the pre-operative ones. Eusterman and Balfour (1935) said from the Mayo Clinic that few total gastrectomies lived more than two years, though they quote that in 1907 Moynihan performed one who lived three years seven months and in 1911 Zikoff did one who lived four years eight months. It is interesting that of the 1,486 Birmingham cases already quoted, the 24 cases who lived over three years were treated by partial gastrectomy only but, then, a number of these were ulcer-cancers, and were probably early cases.

## REFERENCES

- EUSTERMAN, G. B., and BALFOUR D. C. (1935) *Stomach and duodenum*. London.  
 FINSTERER, H. (1947) *Wien. Klin. Wschr.*, 59, 17–22.

**Mr. Reginald C. B. Ledlie :** I propose to summarize the results of a small series of cases of cancer of the stomach at the Royal Cancer Hospital, London, and to show a cine-film of the abdomino-thoracic operation.

During the period 1938–47, a total of 112 cases was referred to me.

Laparotomy was carried out in 84, and resection was feasible in only 29 cases, the resectability rate being just over 25%. The analysis of the five-year results is as follows :

TABLE I.—1938–42

|                           |    |                                               |   |                         |
|---------------------------|----|-----------------------------------------------|---|-------------------------|
| Gastrectomy .. .. .       | 12 | 5-year survivals = 5<br>following gastrectomy | { | 10 years alive and well |
| Radon seeds .. .. .       | 9  |                                               |   | 9 years alive and well  |
| Laparotomy .. .. .        | 9  |                                               |   | 8 years alive and well  |
| Not operated upon .. .. . | 8  |                                               |   | 7 years alive and well  |
| Total                     | 38 |                                               |   | 7 years died of cancer  |

Professor R. A. Willis has kindly reviewed the sections from the cases which survived more than five years, and confirms the fact that they were all undoubted and extensive cancers, with lymph-node involvement in 3 out of the 5 cases.

Every effort was made to resect a higher percentage of cases during 1948.

First, in the course of 206 gastrectomies for peptic ulcer carried out by me at various hospitals, 4 unsuspected ulcer-cancers were found and resected.

Secondly, the abdomino-thoracic approach has been employed for more extensive cancers. This has facilitated removal of the entire stomach when occasion demanded, together with its adnexa and the spleen. The lower end of the œsophagus, the left lobe of the liver, the central tendon of the diaphragm or most of the body of the pancreas have, in addition, been removed in different cases, without affecting the issue of the operation.

The hazards of thoracotomy have been eliminated by modern anæsthetic techniques with the aid of penicillin. 14 of our 15 patients submitted to abdomino-thoracic resection were ambulatory when discharged from hospital. The only one who succumbed from the operation died on the twenty-first day from a leaking œsophago-jejunal end-to-end anastomosis.

Great credit is due to my anæsthetists, Dr. Aileen Chester and Dr. C. B. Lewis, who have enabled us to embark on these formidable procedures with complete confidence in their ability to sustain the vital functions, both during the operation and in the critical post-operative period.

The patients were anæsthetized with intravenous pentothal, followed by endotracheal nitrous oxide and oxygen. Intravenous curare was used to produce muscular relaxation and controlled respiration has been employed throughout. At the end of the operation, aspiration bronchoscopy has been carried out as a routine.

The usual operation time has been within two hours, but in each of the 2 cases in which most of the left lobe of the liver was removed the time was prolonged to two and a half hours.

The alimentary tract is restored by transection of a loop of jejunum, closing the distal end and joining the side of this portion to the end of the œsophagus. The proximal jejunum is implanted in the side of the distal part.

The post-operative course has been remarkably smooth and by the tenth day the patient is eating a liberal diet including mince, chicken, potatoes, greens and milk puddings, and

enjoying stout or ale with his food. During the subsequent months there has been an increase in weight ranging from 8 lb. to 2½ st.

The film portrays 10 men who have undergone abdomino-thoracic resection for cancer of the stomach and are enjoying a square meal.

The majority of these men have returned to their usual occupations and have emphasized the fact that they are capable of enjoying life to the full. The absence of the stomach has in no way diminished their zest for food and drink.

The resectability rate during 1948 was raised to more than twice that of the preceding ten years and now stands at 60% (see Table II).

TABLE II.—1948

| TABLE II.—1948      |    |    |       |    |          |
|---------------------|----|----|-------|----|----------|
| Gastrectomy         |    |    |       |    |          |
| Abdomino-thoracic.. | .. | .. | ..    | 11 | } 18=60% |
| Abdominal ..        | .. | .. | ..    | 7  |          |
| Radon seeds ..      | .. | .. | ..    | 6  |          |
| Laparotomy ..       | .. | .. | ..    | 3  | } 12=40% |
| No operation ..     | .. | .. | ..    | 3  |          |
|                     |    |    |       | 3  |          |
|                     |    |    | Total | 30 |          |

[May 4, 1949]

MEETING AT NORTH MIDDLESEX HOSPITAL, SILVER STREET, LONDON, N.18

## CASES

**Mr. Ivor Lewis :** *Stricture of œsophagus.*

(a) *S. S. (M) aged 57 years. Peptic œsophagitis after milk drip (intubation) treatment of duodenal ulcer.*

Œsophagoscopy: a soft spongy-looking constriction at 36 cm. X-ray: stricture 2 in. long—very narrow. Laparotomy, gastrostomy, retrograde passage of endless silk string for dilatation.

(b) *C. E. (F) aged 3 years. Congenital stricture.*

Dysphagia for liquids and solids present since birth. Opaque swallow and œsophagoscopy show a stricture in distal half of the œsophagus. It feels to be about 1 in. long. Being dilated with bougies every three weeks. No other abnormality found.

**Mr. R. A. Gill :** *Traumatic aneurysm.*

(a) *E. P. (M) aged 39 years.*

Incised knife wound left forearm: sutured 12.3.49. On 29.3.49 noticed swelling at wound site. Some tingling felt along ulnar border. No ulnar nerve lesion.

(b) *C. B. L. (M) aged 53 years. Sarcoma of ankle.*

Tender fluctuant swelling over external malleolus. Very faint pulsation. No bruit. No emptying. Main vessels palpable. X-ray ankle: some decalcification and slight periosteal reaction lower end of tibia and fibula. W.R. and Kahn negative. Gradual increase in size over following six weeks. X-ray of chest shows secondary deposits. I.V.P.—normal kidneys.

**Mr. R. A. Gill :** *Perforation in gastric carcinoma.*

(a) *T. L. L. (M) aged 42 years.*

Partial gastrectomy with recovery.

(b) *V. H. (M) aged 50 years.*

Partial gastrectomy with recovery.

*W. F. C. (M) aged 47 years. Cervical disc prolapse.*

Laminectomy, removal of prolapse, recovery.

Mr. Ivor Lewis : "*Hernia magna.*"

(a) *I. W. (F) aged 70 years. Vast incisional hernia.*

Huge, pendulous, bilocular hernia through a lower mid-line scar of fifteen years' duration, causing recurrent attacks of abdominal pain and vomiting. Repaired at two operations.

(b) *A. C. (M) aged 62 years. Huge recurrent oblique left inguinal hernia.*

Recurrence two years after original repair ten years ago. Hernia reached half-way to knees. Irreducible. 7.7.48. : Repair of hernia.

(c) *H. S. (M) aged 50 years. Huge oblique right inguinal hernia.*

Of twelve years' standing; scrotum 20 in. circumference. 2.2.49 : Classical Bassini repair.

Mr. H. A. Daniels : *Hernia through linea semilunaris.*

(a) *T. H. G. (M) aged 66 years. Left-sided.*

Admitted with tuberculous left testicle : excised. Also has a hernia through linea semilunaris low on left side. Operation refused.

(b) *D. W. (M) aged 56 years. Right-sided.*

Hernia present for fourteen years. Operation. Repair excellent.

Mr. Ivor Lewis : *D. H. (F) aged 44 years. Cyst of common bile duct.*

Excision of cyst plus gall-bladder. Good recovery.

Mr. H. A. Daniels : *D. E. T. (F) aged 39 years. Submaxillary tumour ("mixed" salivary).*

Mr. Ivor Lewis : *H. L. (M) aged 62 years. Pancreatectomy for carcinoma.*

Excision of head of pancreas for carcinoma. One-stage pancreatectomy.

*M. H. (M) aged 46 years. A new way of preventing massive pulmonary embolus.*

Partial compression with silver wire to flatten the femoral veins. This prevents the passage of an embolus large enough to be lethal.

*C. C. H. (M) aged 14 years. Sarcoma of bronchus (1947, Proc. R. Soc. Med., 40, 119).*

Treated by radiotherapy.

Has remained perfectly well for three years and is becoming a sailor.

*M. K. (M) aged 56 years. Calcified plaque of a vaccination scar.*

Vaccinated in Leiden, Holland, when he was about 3 years old—intradermally?

*Spontaneous pneumothorax, with different ætiology and different lines of treatment.*

(a) *H. L. E. (M) aged 26 years. Division of adhesion by thoracotomy.*

(b) *E. B. (M) aged 48 years. Excision of emphysematous bullæ.*

(c) *A. L. (M) aged 39 years. Multiple adhesions, treated by thoracotomy and division of all the adhesions.*

(d) *W. S. (M) aged 35 years. A late case of spontaneous hemo-pneumothorax. Open thoracotomy and decortication of lung.*

Mr. B. H. Page : *Crush injury of abdomen (a) and (b).*

(a) *F. C. (M). Rupture of superior mesenteric vein.*

Crushed between lorries. Signs of ruptured abdominal viscus. At laparotomy rent in superior mesenteric vein was found and sutured. Uneventful recovery.

(b) *T. A. B. (M) aged 7 years. Rupture of liver.*

Run over and trampled by horse. Signs of ruptured abdominal viscus. At laparotomy rupture of liver found and sutured. Uneventful recovery.

(c) *S. D. (F) aged 15 years. Low-grade osteomyelitis of femur simulating Ewing's tumour.*

**Dr. D. Ferriman :** *M. M. (F) aged 36 years. Tetany after thyroidectomy.*

Thyroidectomy (elsewhere) July 1948. Headache since. Epileptiform attack February 1949. Blood calcium 5 mg. per 100 c.c. then. Relief with calciferol and calcium.

*Adenoma of islets of Langerhans.*

(a) *W. B. (M) aged 56 years.*

Periods of abnormal behaviour, "fits" and attacks of coma. Removal of tumour. Recovery.

(b) *S. S. (M) aged 72 years.*

Faintness on heavy exertion for fifty years. Abnormal behaviour before breakfast twenty years. Two recent attacks of coma, one relieved by glucose. Very low blood sugar on fasting. Declines operation.

**Mr. P. F. Jones :** *J. D. aged 4 years. Branchial cyst in child of 4.*

Several months' history of recurrent discharge from a lump in the right side of the neck. Physical signs of cystic inflamed swelling in front of and deep to middle of sternomastoid muscle. X-rayed after injection of diodone. (Confirmed later at operation.)

**Mr. Ivor Lewis :** *D. M. (F) aged 2 years. Congenital atresia of colon.*

(Obstruction in left part of transverse colon when three days old.)

Treated by exteriorization of gut ; closure of colostomy fourteen months later.

**Dr. R. B. N. Wilsdon :** *W. O. (M) aged 36 years. Chronic constrictive pericarditis.*

**Mr. R. A. Gill :** *A. D. (F) aged 79 years. Breast tumour of long duration.*

15 years' history of lump in left breast. Slow increase in size. No discharge from nipple. No pain in breast. Recent pain of sudden onset in left humerus.

On examination : left breast occupied by hard, part solid, part cystic, tumour. Hard mass in axilla. X-rays show recent deposits in humerus and shoulder girdle.

**Dr. J. F. Heggie :** PATHOLOGICAL DEMONSTRATION.

**Dr. E. E. Holdsworth :** RADIOLOGICAL DEMONSTRATION.



## Section of Otology

President—R. SCOTT STEVENSON, F.R.C.S.Ed.

[May 6, 1949]

### Recent Developments In Auditory Tests

By S. RICHARD SILVERMAN, Ph.D.

*Director, Central Institute for the Deaf, St. Louis, Missouri*

IN the past decade interest in clinical auditory tests has been greatly stimulated by a wide, albeit not wholly unrelated, variety of factors. The more significant among these are the development of electro-acoustic instruments which make possible increasingly refined measurements, the growing interest in the fenestration operation, the expanding consumer acceptance of improved hearing aids, the evolution of promising techniques of research in psychoacoustics and finally, but none the less stimulating, the encouraging co-operative attack by workers from allied fields on the problems presented by aural rehabilitation.

From the point of view of the clinical techniques which they employ auditory tests fall into three broad categories: (1) tuning forks; (2) pure tone audiometry; (3) articulation tests. Although the evolution of these tests overlap somewhat in time, the order in which they are stated represents basically the sequence of their development. The historical development and the clinical limitations of tuning fork and pure tone audiometric techniques have been adequately described by Bunch [1] and others and the fundamental principles underlying their application are well known. On the other hand, the basic principles of articulation testing have not universally been implemented in routine otological practice, probably because of the recency of their emergence, the lack of standardization of operating techniques and the unavailability of instrumentation. It is the purpose of this paper, therefore, to deal with the principles underlying articulation tests<sup>1</sup> and to suggest how the results of the tests may be applied to clinical situations.

#### THE ARTICULATION FUNCTION

The articulation function is the basic concept involved in articulation testing. Essentially, it expresses the relationship between the percentage of speech units (syllables, words, sentences) heard correctly and the intensity of the speech at the ear of the listener. The notion of the articulation function grew out of the attempts by Fletcher [7, 8] and his associates at the Bell Telephone Laboratories to devise methods of assessing the efficiency of telephone systems in transmitting speech. The use of speech as the test material was a logical procedure since the purpose of the telephone obviously is to transmit speech. An example of one of Fletcher's early articulation functions is given in fig. 1 [8]. It is seen that as the speech gets more intense the listener hears more syllables correctly. A simpler form of articulation function is shown in fig. 2 [11]. The ordinate shows the articulation score in

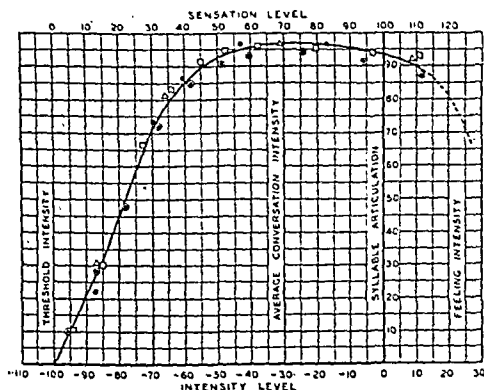


FIG. 1.—Articulation vs. Intensity of Received Speech (see ref. 8, Fletcher, Bell Telephone Laboratories).

<sup>1</sup> Promising tests for young children suspected of deafness using conditioning and electrical techniques are beyond the scope of this paper.

percentage of words repeated correctly and the abscissa gives the relative intensity in decibels. In this case, a list of 50 phonetically balanced words (recognized as proportionately representative of the phonetic elements of normal spoken English) is presented to the listener at enough levels, 10 db apart, to complete the function. A subject is, therefore, credited with

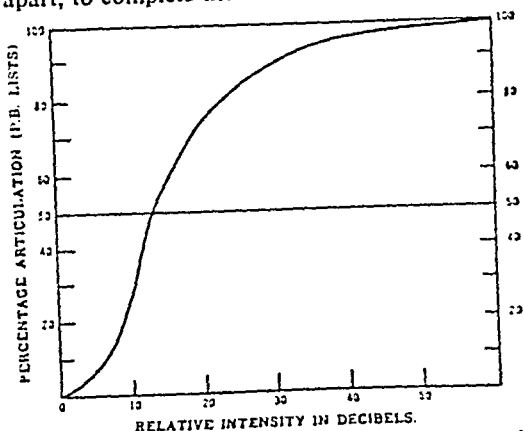


FIG. 2.—Articulation function for normal ear showing increase in percentage of words repeated correctly with increase in intensity (see ref. 11).

2% on the vertical axis for each word repeated correctly. Note also the manner in which the articulation score climbs as a function of intensity—especially the steepness of the slope and the 30 to 40 db range over which almost maximum articulation is achieved.

It is apparent that articulation scores (and functions) are subject to the influence of many variables and care should be taken to hold conditions as constant as possible in making tests except, of course, for the item under test, be it a communication system or an ear suspected of hearing impairment. Miller [10] summarized some obvious, but by no means exhaustive, factors which may affect articulation results, as follows:

- |                          |                                                                                                                                                                                                                |
|--------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <i>Announcer</i>         | Quality and intensity of voice.<br>Correctness of pronunciation.<br>Manner of holding microphone, &c.                                                                                                          |
| <i>Speech</i>            | Phonetic composition and item difficulty.                                                                                                                                                                      |
| <i>Microphone</i>        | Frequency-response characteristics.<br>Non-linear distortion.<br>Efficiency and impedance.                                                                                                                     |
| <i>Amplifier</i>         | Directionality (shielding of microphone from noise—signal-to-noise ratio).<br>Frequency-response characteristics.<br>Non-linear distortion.<br>Input and output impedances.<br>Gain.<br>Peak power-limitation. |
| <i>Earphones</i>         | Shielding (noise pickup and feed-back).<br>Frequency-response characteristics.<br>Non-linear distortion.<br>Efficiency.                                                                                        |
| <i>Earphone mounting</i> | Acoustic seal at the ear (insulation against noise).                                                                                                                                                           |
| <i>Listener</i>          | Air volume under receiver.<br>State of hearing (deafness).<br>Masking of speech by noise entering ear.<br>Basic ability to understand speech when distorted and masked.                                        |

For example fig. 3 [10] illustrates how distance from lips to microphone may influence the per cent word articulation.

#### DETERMINATION OF THE THRESHOLD OF HEARING BY ARTICULATION TESTS

It is well at the outset to clarify the concept of the threshold as it is derived from articulation tests. Three thresholds can be differentiated: (1) *the threshold of detectability*—defined as the point where the listener is just able to detect speech sounds about half the time and where he is not ordinarily able to identify any of the sounds themselves; (2) *the threshold of perceptibility*—defined as the point where the listener begins to perceive some words but where he can barely follow the gist of connected speech; (3) *the threshold of intelligibility*—defined as the point where the listener understands half the material presented to him and where he can presumably follow without perceptible effort the gist of connected speech. Miller [10] has shown that the threshold of detectability lies 7 db below the threshold of

perceptibility and the latter lies 4 db below the threshold of intelligibility. For our purposes in the clinical context we shall need only the threshold of intelligibility.

In constructing a test to determine the threshold of intelligibility Hudgins *et al.* [9] suggest that the test items should meet the following criteria: (1) *familiarity*—the vocabulary should

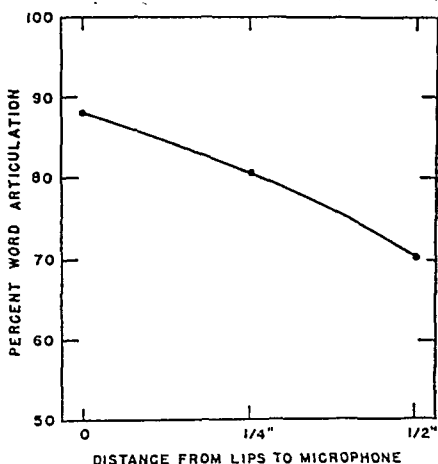


FIG. 3.—Showing the effect on communication of varying the distance of the microphone from the lips. The tests with the announcer and crew of listeners in an airplane noise (115 db). Each point is based upon the average of tests read by three announcers (see ref. 10).

be within the intellectual ken of the listener; (2) *phonetic dissimilarity*—fine discriminations (*cowboy, plowboy*) should not be necessary since no useful purpose is served by them in threshold tests; (3) *normal sampling of English speech sounds*—not essential for threshold testing but a reasonable sampling is desirable; (4) *homogeneity with respect to basic audibility*—the ease with which test words are understood should be as equivalent as possible so that small numbers of items can be scrambled and the articulation function will rise steeply over a narrow range of intensity.

A test which meets these criteria has been developed by Hudgins *et al.* [9] at the Psycho-Acoustic Laboratory of Harvard University. It consists of two lists of 42 dissyllabic words of the spondee stress pattern, i.e. words such as *earthquake, hardware*, in which both syllables are equally accented. The subject hears six words at given levels progressively attenuated in 4 db steps. The point at which he repeats correctly 3 (half) words is the threshold of

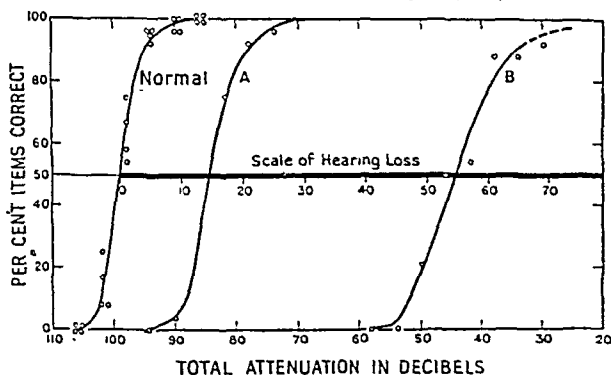


FIG. 4.—Showing how the hearing loss for each of two subjects, A and B, is established in terms of the articulation function obtained from a group of normal listeners. Hearing loss is equivalent to the horizontal distance (in decibels) between the curve for the normal and that for the defective ear. Since the threshold is based on the normal score for 50% correct, the horizontal line through the middle of the plot provides a scale of hearing loss (see ref. 9).

hearing (by our previous definition). Viewed from the standpoint of hearing impairment, the hearing loss can be defined as the number of decibels more required by the impaired ear to hear the equivalent number of words (3). Fig. 4 [9] shows the hearing losses of two

ears of different subjects. Subject A has a hearing loss of 14 db and subject B a loss of 55 db. In other words, subject A requires 14 db and subject B 55 db more than the normal ear to hear the same number of words. The spondee test is usually referred to as "Test No. 9".

A sentence test (No. 12) based on the same principles as the No. 9 has also been developed by Hudgins *et al.* [9]. It consists of 8 lists of short, simple questions, each of which can be answered with a simple word. The lists are composed of 28 items divided into seven groups of four items each, with each group of items given at progressively attenuated steps of 4 db.

The relationship of per cent word articulation and sentence intelligibility depends, of course, upon the type of words and sentences used. A fairly typical curve of this relationship plotted by Egan [5] is given in fig. 5. Hudgins *et al.* [9] found that the threshold for

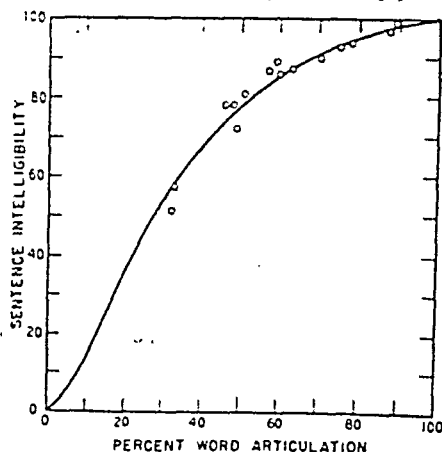


FIG. 5.—Lists of words and lists of sentences were compared as to intelligibility under a wide variety of conditions. Each point on the graph represents one test of 100 words and one test of 50 sentences. The curve passing through the data was derived from results obtained at the Bell Telephone Laboratories (see ref. 5).

the No. 12 (sentence intelligibility) test is about 4 db above the threshold for No. 9 (spondees).

Another speech test (not using the concept of articulation function) has been described by Falconer and Davis [6]. In this test the subject listens to a sample of recorded connected discourse and manipulates the attenuator until he just is able to get the gist of what is being said. His hearing loss is the number of decibels more which he requires than the normal ear to reach his threshold of intelligibility for connected discourse. This test has the advantage of economy of time and high face validity. The end-point, on the other hand, is relatively not too definitive. However, Thurlow, *et al.* [16] found that hearing losses for speech that only one of them need be used in any clinical routine.

#### TESTING AUDITORY DISCRIMINATION

It is not only important to determine the faintest speech which an ear can hear (measured by threshold type tests described in the previous section) but it is of great clinical significance (as we shall point out later) to know how the ear hears speech at any intensity, particularly above threshold. Clinicians are familiar with the patient who says "I hear, but I can't understand; I can hear better if you speak clearly rather than loudly". This patient's problem is not sharply delineated by the threshold tests. Granted that a sound needs to be audible before it can be distinguished from the other sounds, the fact that it is audible does not necessarily guarantee that it can be recognized accurately. The ability to distinguish one sound from another when both are audible is called *discrimination* as distinguished from *sensitivity* which refers to the faintest sound which the ear can hear. In addition to sensitivity, a high degree of discrimination is needed to discriminate *sin* from *thin* and *pit* from *pith*.

In constructing a test to measure the power of discrimination (or, clinically, the discrimination loss) Egan [5] suggests the following criteria: (1) *representation of fundamental speech sounds*: reasonable proportional representation in the test lists of the sounds that occur in everyday speech insures that the test measures what it sets out to measure, i.e. how the ear copes with the task of discriminating speech which it is likely to have to discriminate

in routine oral communication; (2) *types of test items*: words appear to be preferable to nonsense syllables which may require recording by phonetic symbols and to sentences which may afford contextual clues; (3) *difficulty and reliability test lists*: the test items must be so selected that the distribution of item difficulty in each list will make possible a sensitive measuring instrument. In other words, those items which under conditions of the tests are always recorded correctly, or are always missed, should be eliminated from the test lists. Of course, for both sensitivity and discrimination tests many equivalent lists should be available to cut down the learning factor when more than one test is necessary.

Egan [5] and his associates at the Psycho-Acoustic laboratory have constructed a test which meets fairly adequately the criteria for discrimination tests mentioned above. This test consists of 20 equivalent phonetically balanced lists of 50 words each. Fig. 2 [11] shows the articulation function which is derived from the P.B. (phonetically balanced) lists. The discrimination loss, measured along the vertical axis, would be the percentage of words less than 100% which the ear could discriminate at an intensity level sufficiently high above threshold to eliminate the factor of questionable sensitivity. In other words, no matter how loud the speech is made, the ear may still fail to discriminate all of the test words.

A comparison of the shapes of the No. 9 and P.B. curves taken from Davis [2] is shown in fig. 6. Notice that the spondee curve rises steeply because the words are almost equally

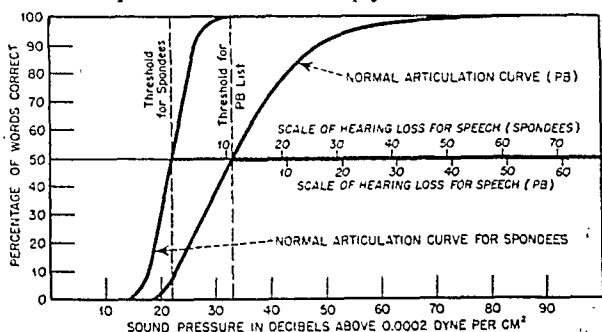


FIG. 6.—Showing difference in slopes of two types of articulation curves (see ref. 2).

audible while the P.B. curve rises more gradually because the words represent the broad range of difficulty encountered in everyday speech.

*Tests of tolerance.*—Tests of tolerance for loud sounds are helpful in the clinical selection of hearing aids. It is important that a patient use a hearing aid with an acoustic output which approaches but does not exceed his threshold of discomfort as described by Silverman [12].

The test for tolerance is fairly simple. The subject listens to connected speech and he is instructed to increase the intensity until the sound just becomes uncomfortably loud. This point on the intensity scale is his threshold of discomfort.

#### CLINICAL APPLICATIONS OF ARTICULATION TESTS

Articulation tests, properly applied, serve a useful purpose for the clinician who is confronted routinely by problems of diagnosis, prognosis and evaluation of medical and surgical procedures and hearing aids.

(1) *Diagnosis and prognosis.*—The otologist is called upon routinely to differentiate between deafness of the conductive and nerve types. Or, in other words, he must assess cochlear function. The patient who is a candidate for fenestration surgery is a case in point. We can test the patient with the P.B. lists at high intensity levels (free from distortion) and if his articulation score increases proportionately with intensity (as the score in the function shown in fig. 2) he has adequate cochlear function. In essence, an attempt is made to accomplish prior to surgery what the surgery sets out to do—namely, to deliver sound to the analysing mechanism in the inner ear by over-riding or by-passing a conductive lesion. If the attempt to deliver sound over the electro-acoustic system is successful as judged by the maximum articulation score, then surgery, intended to alter beneficially the transmission mechanism of the ear, should accomplish the same result.

In fig. 7 we see unsmoothed articulation functions taken from the clinical records of Walsh and Silverman [17]. Curve A is that of a patient who reaches a relatively high maximum articulation score if presented with speech at high intensity. This patient, therefore, has adequate cochlear reserve and would be a good candidate for surgery. Curve B represents a patient with mixed deafness, since his articulation score does not rise with intensity in the

same manner as curve A. The conductive aspect of his deafness might be helped by fenestration but his prognosis would be less favourable than that of the first patient. Note that in curve C increasing the intensity does not proportionately elevate the articulation score after a certain maximum has been reached. The curve of this patient shows that adequate cochlear function is not present. Surgery might provide for more sound to be delivered to the inner ear, but lack of adequate cochlear reserve would preclude reception beneficial to the patient. Walsh and Silverman [17] point out further that the thresholds of the three curves are practically identical but the diagnosis and prognosis are based on auditory func-

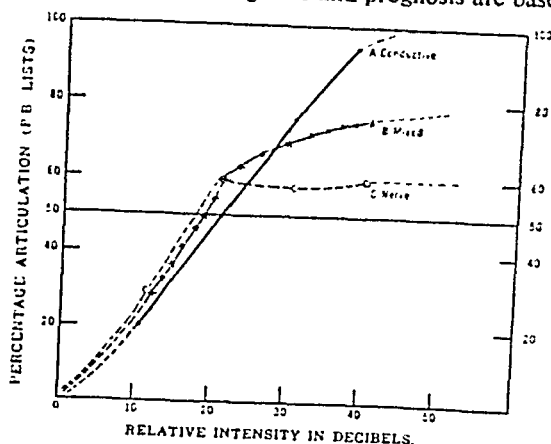


FIG. 7.—Showing articulation curves for conductive, mixed and nerve type deafness (see ref. 17).

tion above threshold; consequently, prime significance is attached to the *shape* of the articulation function and particularly to the *maximum articulation score*. Davis *et al.* [3] in their investigation of design objectives for hearing aids related maximum articulation scores to clinically determined types of deafness and confirmed the notions of Walsh and Silverman.

It is clear, too, that the maximum articulation score enables us to predict the value which a patient might derive from a hearing aid. Although a hearing aid might shift the curve to the left it cannot be expected to raise the maximum articulation score since the latter is dependent upon the integrity of the cochlea. The hearing aid enables the user to hear easier what he already can discriminate but it does not add new powers of discrimination. It has

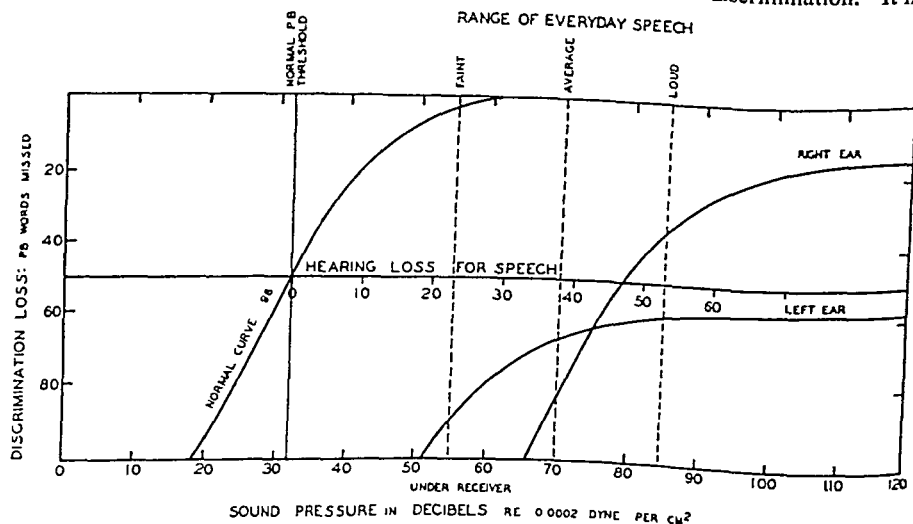


FIG. 8.—Showing the difference in both sensitivity and discrimination scores in two ears of same subject. Sensitivity is measured along the horizontal axis and discrimination along the vertical (see ref. 13).

the effect of bringing the talker closer to him. Incidentally, this may be helpful for the alert user, since it frees him from the necessity for straining to hear faint sounds and permits him to make use of contextual clues to understand connected speech. Auditory training is helpful in developing this power of synthesis.

The articulation score is helpful in the choice of ear for the use of a hearing aid particularly where both the threshold and maximum articulation scores differ from ear to ear in a given patient. An interesting illustration is shown in fig. 8 [13]. This patient, from our hearing clinic, has good sensitivity but poor discrimination in the left ear and poor sensitivity and good discrimination in the right ear. Since his discrimination was good in the right ear, it was a simple matter to override his deficiency in sensitivity with a good hearing aid and to retain adequately his power of discrimination. It is obvious that a hearing aid in his left ear would not have been too helpful because of its difficulty in discriminating as

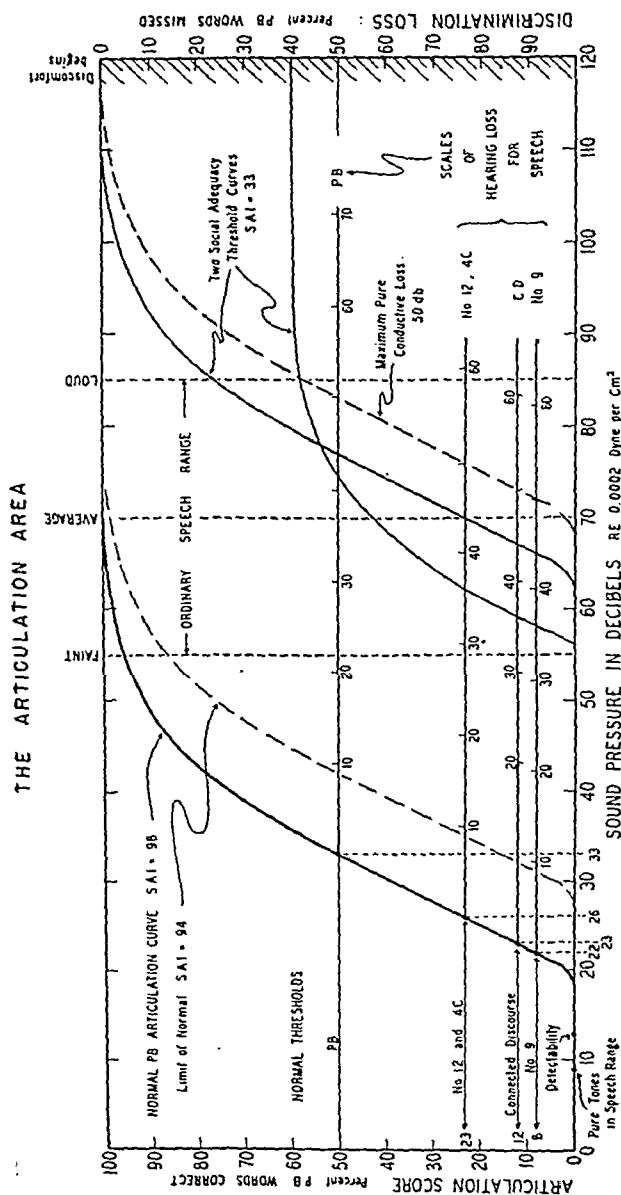


FIG. 9.—Version 1—February 1, 1948. These curves are based on the P.B. word lists of the Psycho-Acoustic Laboratory as recorded at Central Institute for the Deaf (Spoken by Rush Hughes) and used with the electro-acoustic installation in Laboratory No. 2 at Central Institute for the Deaf as of January 1948.

The other thresholds are for recorded tests, used with the same apparatus, as follows: No. 9 (spontaneous words) and No. 12 (sentences): Psycho-Acoustic Laboratory, Harvard. 4C: (2-digit numbers): Western Electric Co. Connected Discourse (thresholds of intelligibility and detectability), newcast by Fulton Lewis, Jr.: Central Institute for the Deaf.

The Social Adequacy Index is the average percentage of P.B. words that would be correctly understood by the patient at the three speech levels indicated by the dotted lines.

Hearing loss may be conductive, perceptive or both. Fenstermaker can offset only the conductive element of hearing loss. The maximum purely conductive loss is probably 50 db. Hearing aids can offset the "hearing loss for speech" but they do not improve discrimination (see ref. 4).

demonstrated by the maximum articulation score. Similar application of these principles can be made to the choice of ear for the fenestration operation.

(2) *Evaluation and the concept of social adequacy.*—In order practically to evaluate therapeutic procedures and hearing aids we generally need to know to what extent we have improved the patient's ability to cope with the everyday dynamics of oral communication.

To this end Walsh and Silverman [17] suggested the concept of the *social adequacy index for hearing (SAI)* which essentially is the average percentage of P.B. words that would be correctly understood by the patient at the faint, conversational and loud speech levels. In other words, just as we are accustomed to averaging hearing loss at critical frequencies, we average ability to hear speech at critical intensities, in this case determined by social criteria. The threshold measure is not in itself adequate to predict a patient's performance since we have seen that ability to discriminate speech can vary widely above threshold in patients who may have the same threshold scores. The SAI, on the other hand, evaluates our remedial measures in terms of shifts both in sensitivity and discrimination. It tells us, for example, that the patient with poor discrimination is not helped by shouting, as we must in a noisy place, because an increase in intensity does not improve his power of discrimination. In a sense, the SAI accounts for hearing performance in a dynamic acoustic environment.

Davis [4] has elaborated the motion of the SAI and has brought into quantitative relationship the various articulation tests. This is shown in fig. 9. He has also presented a table for the rapid calculation of the SAI.

Frequently, clinicians evaluate measures to improve hearing by soliciting a subjective judgment from the patient as to the status of his hearing. Silverman *et al.* [14] studied the relationship in a series of 161 fenestration patients between their judgments of the status of their hearing and articulation tests performed under laboratory conditions. The patients were furnished a rating scale for various conditions under which they had to listen in everyday life (noisy places, audience situations, group conversation, &c.). Figs. 10 and 11 [14]

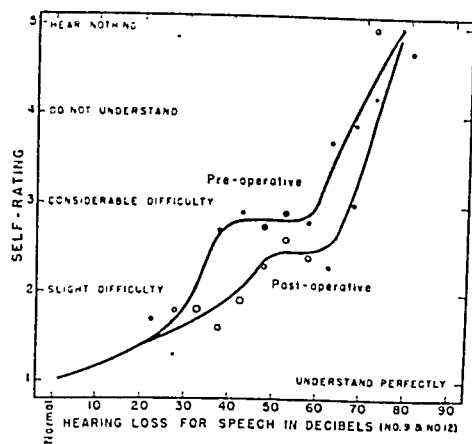


FIG. 10.—Showing relationship between patient judgment and hearing loss for speech (see ref. 14).

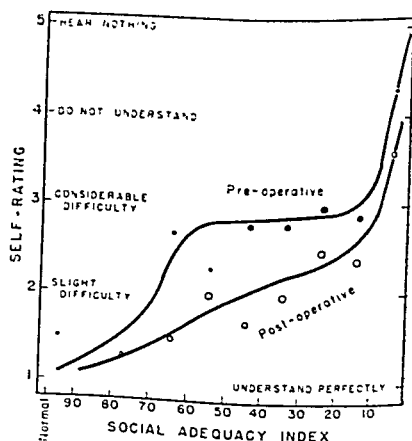


FIG. 11.—Showing the relationship between patient judgment and social adequacy index (see ref. 14).

show the relationships between patient judgments and actual measured losses and SAI scores respectively. Theoretically, we should expect linear relationships, i.e. the greater the hearing loss (or the lower the SAI) the greater difficulty in hearing as judged by the patient. The plateau in both curves indicates that this is not so, probably because it is possible to compensate by the raised voice for losses of hearing up to 60 db. Note, too, the changes in judgments post-operatively. At any rate, patient judgment as a technique of evaluation should be employed with extreme caution. The table below, from Silverman *et al.* [14], indicates the numbers in terms of hearing loss and SAI which may be placed on certain critical social thresholds. Incidentally, this information may be useful to those who must deal with job classification and medico-legal problems.



## THRESHOLDS OF HEARING

| Threshold                                                              | Db loss for speech*    | SAI † |
|------------------------------------------------------------------------|------------------------|-------|
| (1) Normal .. .. .                                                     | 0                      | 98    |
| (2) Limit of normal .. .. .                                            | 9 <sup>+</sup>         | 94    |
| (3) Social difficulty begins .. .. .                                   | 30                     | 67    |
| (4) Threshold of social adequacy<br>(middle of threshold zone) .. .. . | 45                     | 33    |
| (5) Limit of compensation .. .. .                                      | 60                     | 10-15 |
| (6) Limit of compensation with a hearing aid .. .. .                   | Still to be determined |       |

\* These values apply only to ears with perfect discrimination, i.e. ears that can hear correctly all PB words if they are made loud enough.

† The Social Adequacy Index takes into account loss of discrimination as well as loss of sensitivity.

‡ This limit is three times the standard deviation for a group of normal listeners.

## EQUIPMENT

Equipment for the administration of articulation tests ranges from the simple to the elaborate. In fig. 12 we see a simple arrangement of equipment suggested by Hudgins *et al.* [9] for the administration of recorded articulation tests. Fig. 13 shows a more versatile and elaborate assembly of electro-acoustic equipment for clinical auditory tests suggested by Silverman and Harrison [15]. It cannot be emphasized too strongly that whatever equipment is used, *its characteristics should be known, it should be accurately calibrated (both physically and on human subjects) and it should be checked periodically for consistency of performance.* It is likely that simple, inexpensive assemblies of standardized equipment will soon be available and within reach of the practising otologist but even when this comes to pass the above precautions must be observed. After all, articulation scores are relative scores contingent upon the variety of factors mentioned previously. Only relative statements can be made about them within a framework of accurately described equipment and conditions.

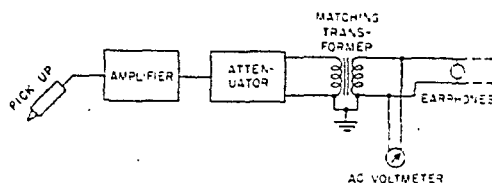


FIG. 12.—Arrangement of the equipment for administering the auditory tests (*see ref. 9*).

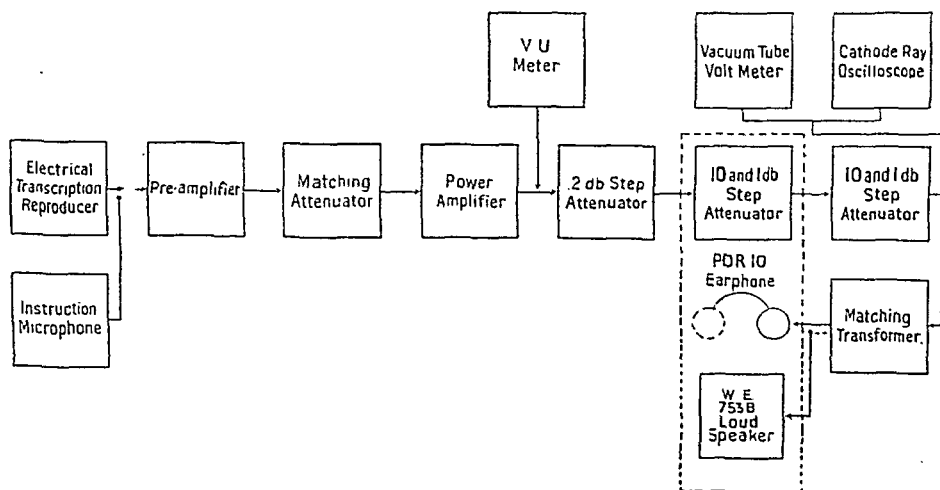


FIG. 13.—Block diagram of suggested assembly of electro-acoustic equipment for clinical auditory tests (*see ref. 15*).

The question of live voice versus recorded (with known characteristics) articulation tests arises when procurement of equipment is being considered. The answer is by no means definitive or conclusive. In general, live voice tests have the advantage of economy, since no turntable or expensive recordings are required. In addition they eliminate a source of error which might creep in from a poor reproducer or inferior recordings. The tester can also vary the material. On the other hand, recordings have the great advantage of insuring uniformity of test material from test to test and their use does not fatigue the tester who in the live voice situation must concentrate on some form of monitoring device. Research is under way to compare the reliability and efficiency of both techniques.

Finally, workers in the field of articulation testing must not be reluctant to concede that articulation testing, at least in the present state of the art, should be viewed critically and, in some instances, experimentally. Ongoing research says that articulation tests need to be increasingly refined and validated and they need to be further streamlined for wider clinical application. Certainly this can be said about most clinical techniques. Articulation tests are not intended to supplant orthodox clinical tests but they are a valuable supplement and they should hold a respectable place in the armamentarium of the clinical otologist because they are quantitative, reproducible, reasonably valid and they tend to objectivize the response of the patient. After all, in articulation testing the patient either repeats the word correctly or he does not. He cannot get by with "maybe".

#### TOPICAL SUMMARY

- (1) Progress has been made in the last decade in the development of articulation tests for clinical purposes.
- (2) The principles underlying the articulation function which expresses the relationship between words correctly heard and intensity are discussed.
- (3) The articulation test as a measure of sensitivity (hearing loss) and discrimination is described.
- (4) Tests of tolerance for loud speech are discussed briefly.
- (5) How the articulation test may assist in diagnosis and prognosis is shown.
- (6) The use of the social adequacy index for evaluation of remedial procedures is described.
- (7) Comments are made concerning the equipment necessary for the administration of articulation tests.
- (8) Articulation tests serve a useful purpose for the clinical otologist.

#### REFERENCES

- 1 BUNCH, C. C. (1943) *Clinical Audiometry*, St. Louis.
- 2 DAVIS, H. (1947) Ch. 6, *Hearing and Deafness, A Guide for Laymen*, New York.
- 3 —, STEVENS, S. S., NICHOLS, R. H., HUDGINS, C. V., MARQUIS, R. J., PETERSON, G. E., ROSS, D. A. (1947) *Hearing Aids, An Experimental Study of Design Objectives*, Cambridge, Mass.
- 4 DAVIS, H. (1948) *The Laryngoscope*, 58, 761.
- 5 EGAN, J. P. (1948) *The Laryngoscope*, 58, 955.
- 6 FALCONER, G. A., and DAVIS, H. (1947) *The Laryngoscope*, 57, 581.
- 7 FLETCHER, H., and STEINBERG, J. C. (1929) *Bell System Tech. J.*, 8, 4.
- 8 — (1929) *Speech and Hearing*, New York.
- 9 HUDGINS, C. V., HAWKINS, J. E., KARLIN, J. E., and STEVENS, S. S. (1947) *The Laryngoscope*, 57, 57.
- 10 MILLER, G. A. (1946) Ch. 5, Summary Technical Report, N.D.R.C. Vol. 3, Transmission and Reception of Sounds under Combat Conditions, Division 17, Washington, D.C.
- 11 O.S.R.D. Report No. 3802, Articulation Testing Methods, II, November 1, 1944.
- 12 SILVERMAN, S. R. (1947) *Ann. Oto-Rhino-Laryng.*, 56, 658.
- 13 — Determination of the "Better" Ear in Bilateral Impairment of Hearing (In press).
- 14 —, THURLOW, W. R., DAVIS, H., and WALSH, T. E. (1948), *The Laryngoscope*, 58, 607.
- 15 —, and HARRISON, C. E. (1945) *Electro-Acoustic Equipment for Clinical Auditory Tests*, CIDIC-1-O.S.R.D. St. Louis, February 15.
- 16 THURLOW, W. R., SILVERMAN, S. R., DAVIS, H., and WALSH, T. E. (1948) *The Laryngoscope*, 58, 43.
- 17 WALSH, T. E., and SILVERMAN, S. R. (1946) *The Laryngoscope*, 56, 536.

#### DISCUSSION

Mr. T. G. Wilson said that the classical methods of measuring auditory acuity were speech tests and tuning forks. He supposed that they could hardly call audiometry a classical method as its use had only recently become well established. The principal function of the human ear was to hear speech, but the rough and ready methods of testing which had always been employed were unsatisfactory and interest had therefore shifted rapidly to the use of tuning forks. The development of the absolute bone conduction test and the introduction of calibrated forks stimulated increasing interest in their use until about fifteen years ago, when every otologist bought an audiometer and in a lot of cases forgot all about the other methods. But the evolution of fenestration

recently had stimulated interest in all forms of hearing tests, and tuning forks were not so much neglected as they had been.

His own procedure in testing was first of all to use a set of calibrated forks and to make a rough test with the audiometer. He also carried out a rough speech test. On the following day he made careful audiometric records and tested again with tuning forks, and repeated the whole series of tests once more when the patient finally came up for fenestration.

It could be said, comparing the relative merits of forks and of the audiometer, that tuning forks were perhaps most useful for testing low tones and bone conduction, while the audiometer was more useful for high tones. The audiometer lent itself to graphic-recording, but there were many ways of graphically recording tuning fork tests as well. Finally, tuning forks were a better way of making the clinical diagnosis while the audiometer was probably better for the routine checking of progress or of regression in hearing.

Hallpike had shown that patients who exhibited apparently increased bone conduction when tested under ordinary room conditions were found to have normal or subnormal bone conduction when tested in a soundproof room. This finding, of course, clarified the meaning of the bone conduction tests. The hearing of the examiner was diminished in proportion to the background noise; that of the patient was not diminished because he did not hear it.

It had recently been said that when the air-conducted hearing was markedly improved by fenestration, bone conduction was also definitely improved and a small number of cases had been brought forward which appeared to bear that out. If it were true it was an observation of very considerable importance, because it meant that loss of bone conduction due to otosclerosis might prove partly reversible.

In his view audiometry furnished a reliable method of estimating bone conduction though he agreed with Lindsay, of Chicago, who had said that the greatest pitfall in the measurement of bone conduction in otosclerosis had been in masking.

He thought the modern audiometer was reliable and that a very large source of the error was in the human element. A soundproof room and a carefully regulated technique were a great help.

They had come to the conclusion generally that the line of demarcation between perceptive deafness and conduction deafness was not as cut and dried as they had thought. No real advance had, however, been made in the exact localization of the lesions producing deafness, although the investigation of the Loudness Recruitment Phenomenon seemed very promising.

Concerning the subject of speech testing, it would seem that the essence of Dr. Silverman's work could be classified as follows: first of all, control and knowledge of the conditions of the test; secondly, proper selection of the syllables, words, or sentences used, and thirdly, the graphic representation of the results, which were, of course, obtained under proper conditions.

He wondered whether Dr. Silverman had given quite enough attention to the factor of intelligence—not intelligibility, but intelligence. Many quite intelligent people were slow in the "take-up". Farmers, for example, were proverbially slow in picking up, but that did not mean that they were stupid. The education and environment of the patient must be taken into account.

Mr. I. Simson Hall referred to certain difficulties in the standardization of the speech tests. He had recently brought back certain word lists from an organisation in Chicago and gave them to his assistant, but his assistant told him, "I cannot use these unless I use an American accent".

As regards the fenestration procedure, they seemed at times to get results following the operation which seemed completely to negative their previous tests. The cochlea, after being opened, seemed to react quite differently from the way it did before it was opened and doubtless they had a great deal still to learn about the phenomena of conductive deafness.

On the re-education of the patient after fenestration, some patients heard quite differently after the fenestration operation; disorientation might also occur. These results required further research.

Air Commodore E. D. D. Dickson referred to the work undertaken in the early part of the war in the Royal Air Force. Dr. Fry was in great part responsible for the development of certain hearing tests for ascertaining the capability of aircrews to understand speech under working conditions, viz. in a background of noise. The tests were based to a large extent on certain of the conceptions which Dr. Silverman had propounded. The R.A.F. contribution has already been published and described in the *Proc. R. Soc. Med.* (1945) 38, 634, and *J. Laryng. Otol.* (1946) 61, 139. The equipment and testing material has proved useful in evaluating the help likely to be derived from a hearing aid. It is used in their rehabilitation scheme. The man with a high score in a background of noise was likely to benefit from a hearing aid whereas those with a low score would not. Research was proceeding in the field of speech audiometry in estimating the improvement derived from the fenestration operation. The equipment developed and in use in the R.A.F. was based on principles similar to those put forward by Dr. Silverman.

Dr. T. S. Littler said that the speech test was very important. In connexion with the use of a hearing aid there were many points that required investigation. The condition in which articulation and intelligibility did not increase with intensity similar to the normal state, called for further research. In such a condition, when speech is to be reproduced by a hearing aid, it might even be desirable to suppress to some extent the range of frequencies over which the ear was most defective.

Dr. D. B. Fry said that in discussing the "spondee" word-lists, Dr. Silverman had referred to words like "earthquake" and "hardware"; but these words were not equally stressed on both syllables and when one listened to the complete list of words used in the test one found that in not more than about half of them were the syllables equally stressed. They were in fact simply two-syllabled words with a strong vowel in each syllable. What was the real advantage of using such words? When one added the word "quake" to the word "earth", one increased the probability of correct recognition of the whole word, but this seemed only to make the actual test rather easier. Did it in fact increase its reliability? It had been their experience during the war, that one did not get reliable results when using groups of words as small as those used in the spondee test.

The other question he wished to put to Dr. Silverman was whether he and his colleagues had tried using sound articulation tests, that is tests in which credit was given for every sound correctly recognized. They had applied this technique in tests evolved during the war and it had worked well. Other things being equal, one tended to get more reliable results with an increase in the number of test items. He would suggest to Dr. Silverman that if credit were given for every sound correctly received, one could have a shorter test with more test items.

Mr. C. S. Hallpike said that the Electro-Acoustics Committee of the Medical Research Council had been called upon to study the same problems which Dr. Silverman had so ably surveyed.

As the Committee's Report showed, the conclusions reached by the Committee and the test methods elaborated were substantially indistinguishable from those which Dr. Silverman had described. This was encouraging since it showed that the principles upon which these tests were based were clearly defined and well established. They were in sight, he hoped, of a close standardization of their methods on both sides of the Atlantic. There were only one or two points of difference. It appeared that in America spondee words were much used. In England, however, single syllable words were found to be much more serviceable than spondees, and these were used in short lists of 25 words. By that means they found that they were able to carry out many more tests on patients than would have been possible with longer lists.

Dr. Silverman, in reply, agreed that the intelligence of the patient was an important question and allowance must be made for slowness of what had been called "pick up". One must be as ingenious as possible in estimating a person's intelligence and sizing up the patient and his attitude toward the test.

They found the sentence test much more helpful in many clinical cases than the word test or the so-called spondee test. He agreed with that entirely but particularly in the case of elderly people.

Standardization was a critical problem, and with it went reliability and validity. The manner in which these tests were directed and carried out was taken into consideration. They were carried out on many people under well-defined conditions. The mere departure from predicted scores had a certain value. It meant that here was a patient whose case had to be looked into because he departed from standard. Statistics therefore were carefully studied. It was found that increasing the number of test items to get a special test did not materially increase the reliability. He was pleased to know that they were getting reliability on this side and that what they wanted were shorter lists. In the States they were experimenting with the same sort of thing though they had nothing conclusive at the moment. They thought at one time that they could reduce the P.B. list to a dozen words. That was something they were still trying to do.

He was interested in Air Commodore Dickson's comment upon the use of tests in noise for the prescription of a hearing aid. He said that if the patient performed well in noise he would predict better performance with the hearing aid, and he felt that that was a very good approach.

There was one very nebulous thing which in his country they could only call "quality". It might be related to articulation scores but it was very difficult to measure. This was a problem they were now tackling. They could show a case where a person got the same score at an articulation test with two different hearing aids and yet quite definitely preferred one hearing aid to the other.

The question of word lists to which Mr. Simson Hall had referred was, of course, important. He could not answer just what words should be used. He had only tried to indicate the principles. It seemed to him that each country must work out what it considered suitable for its own purposes. It might be that some languages were much easier to hear than other languages.

Concerning his reference to "road block", to which Mr. Simson Hall had alluded, this was just an empirical observation on his part and they were not completely settled as to the physics of the operation.

In connexion with the fenestration operation he would like to suggest an experiment whereby they took a pair of headphones and had them working in phase, asking the patient to localize where the sound was heard. Then one of the phones might be thrown out of phase, whereupon the localization became different. This might be done pre- and post-operatively and some interesting results might ensue. He concluded by remarking that they by no means felt that the problem had been solved.

## Section of Epidemiology and State Medicine

President—Sir ALLEN DALEY, M.D., F.R.C.P., D.P.H., K.H.P.

[May 2, 1949]

### "I Remember"

#### PRESIDENT'S ADDRESS

By Sir ALLEN DALEY, M.D., F.R.C.P., D.P.H., K.H.P.

WHEN the subject of this Presidential Address first confronted me I read the Addresses of many of my distinguished predecessors and was filled with dismay. Each was a master in some branch of work and he prepared a detailed paper on it which discussed the matter in all its aspects and, generally, added new knowledge never before published. I, on the other hand, make no claim to expert knowledge of any particular branch of public health but my range of interest has always been wide. It, therefore, occurred to me that you might not find it entirely devoid of interest if I surveyed briefly the things which in a public health career of nearly forty years have, from time to time, attracted my special attention as, by this means, the ebb and flow of trends and the lessons to be derived therefrom can be discerned. My work has been entirely in urban communities. Nine years as Medical Officer of Health of Bootle, a dockside community adjoining Liverpool; five years in Blackburn, a cotton manufacturing town; five years in Hull, then our sixth largest provincial city and the third largest port, and twenty years in London. My pen has seldom been idle and it seemed to me that a reference to the subjects on which I have written or lectured would indicate what engaged my special attention at the time. To my astonishment I find that, apart from annual reports, I have written 157 special articles, formal lectures, or speeches of which the notes have been kept. Perhaps I should be ashamed at such a disclosure when I reflect on the wearied readers or bored listeners on whom they were inflicted.

As might be expected the earliest dealt with environmental sanitation: the removal of household refuse, housing and overcrowding, rat-proofing and sanitation, and hygienic conditions, including avoidance of eye-strain in places of public entertainment. It is difficult to realize that in 1922 when I wrote the paper last mentioned cinemas were only just beginning to appear and most of them at that time were converted concert halls or theatres.

#### PLAGUE

My paper on "Rats and Their Extermination" in 1913 [1] had a curious development. A summary had appeared in the local newspaper and in it reference was made to the relationship of rats to the spread of plague. A week or two later the police telephoned to ask if I would be interested to know that a number of dead rats had been seen in a street. It was a small *cul-de-sac* flanked on each side by a warehouse. I said I was most interested. I had just persuaded the Town Council to appoint a rat-catcher, or rodent exterminator, as he would now be called, and I sent him to investigate. The dead rats had disappeared but he caught a few live rats in the warehouses and I sent them to the Bacteriological Laboratory of the University of Liverpool for examination. Within a few days I received a telephone message to the effect that one of them was infected with *B. pestis*. Many hundreds of rats were then caught and examined but no further case of rat infection was found. My friend and colleague, Professor E. W. Hope, then Medical Officer of Health of the City and Port of Liverpool, and still happily with us at the age of 95, was, of course, informed. Rats from Liverpool

warehouses were examined and one of them also was found to be plague-infected. Enquiry from the Port Authority then revealed that the only cargo common to the two warehouses where the plague-infected rats had been found was Egyptian cotton received a month or so before. On arrival in Liverpool part of the cargo of cotton had gone to the Bootle warehouse, part to that in Liverpool. There was plague in Egypt at the time. But the story is not yet finished. About three weeks later, a boy was sent into the Liverpool Royal Infirmary with symptoms pointing to appendicitis. On exploration, the appendix was found to be normal but the very careful surgeon—Mr. (later Sir Robert) Kelly—noticed that some of the adjoining glands were enlarged and inflamed. He cut one out and sent it to the laboratory. The next day was Whit-Monday and the Association of Physicians was meeting in Liverpool. The Assistant Pathologist, later a distinguished member of the Public Health Service, called in hurriedly on his way to the meeting to deal with anything really urgent. He did not regard an inflamed abdominal gland as coming within that category but the technician had made a smear from it so the pathologist looked at it and found it contained typical *B. pestis*. He did not get to the meeting! The boy was found to come from a flea-infested house, his father had died suddenly of what was certified as "pneumonia" a fortnight before and he had worked at a paint factory which was next door to the warehouse where the Liverpool plague rat had been discovered. Fortunately there were no further cases, so far as is known, among rats or men.

To revert to my publications, the increasing interest of the public health service in the personal health services is evident. In 1911 I wrote a report on Tuberculosis and Tuberculin Dispensaries following a visit to London where I saw the work done by Drs. R. S. Walker, Halliday G. Sutherland and W. Camac Wilkinson, the last with at least one duchess watching him give injections of tuberculin.

#### HOME HELPS

In 1920 I wrote a paper on Home Helps [2]. I had selected a few women, sent them for three months' experience in a residential nursery so that they might learn how to look after a very young baby, and offered their services to Bootle mothers during their confinements. Almost with one accord, the mothers, who, when asked, had said how much they would like help at this period, having seen the proffered home help, began to make excuses and thought they could manage. I had chosen the home helps because they were smart, good-looking women and enquiry showed that the mothers would have been glad to have them about the house if they were plain, or preferably, positively ugly, or if their husbands had been at sea or for some reason not at home. The few who were acceptably, and better, babies were looked after in the places where they had been "trained". It was not until I was in Hull some years later that I had the courage to start another Home Help scheme. I profited by my experience. They were given no training in child care and good looks were a disqualification. The scheme was very successful and now we can select the best candidates independent of what they look like.

During the first World War one of my jobs was to act as Medical Officer of the two Liverpool Dock Battalions. I gained an insight into the hazards of dock labouring and wrote a paper [3] on the physique and working capacity of the Liverpool Dock Labourer. The average number absent through injury was 7.7 per 1,000 and through sickness 43.7. I was impressed by the need for decasualizing this form of employment which, I am glad to say, has recently been done.

#### HEALTH EDUCATION

Soon after that war I became interested in the education of the public on how they could help themselves to good health by having imparted to them simple facts about how the body works, the infections and the diseases which assail it, the importance of consulting a doctor in the early stages of illness and the public provision made to safeguard health. This is an interest which remains with me still. I wrote much on the subject, including a book [4], and took an active part in the foundation in 1926 of what is now the Central Council for Health Education. I studied the technique of handbills, most of which at that time were deplorable in their set-out and phraseology, posters, health exhibitions and health lectures. There are three types of medical lecturer. The majority who have the basic knowledge but cannot put it into the simple language which the general public can understand. A small number who have a magnificent presence and delivery but who say things which outrage those doctors who believe that the public should be told only "the truth, the whole truth and nothing but the truth". Then there is the *rara avis* who knows both what to say and how to say it. There was in those Northern towns a remarkable avidity for information on health

and audiences of between 1,500 and 3,000 people were attracted to popular lectures. I still believe that the Medical Officer of Health has no function which is more important than the education in health matters of the community which he serves. The great difficulty is to produce material which is strictly accurate without introducing so many provisos that the value of the message is lost. I believe the danger of producing a race of neurasthenics as a result, for instance, of stressing the importance of early treatment in cancer or tuberculosis, has been over-emphasized. If the message is put forward as one of hope if the disease is discovered early, it not only saves lives but also the misery which follows an intimation on the first visit to the doctor that "if you had only come earlier you would have had a better chance of recovery". I have often discussed with philosophers, the clergy and others whether the young adult is more influenced in propaganda work against venereal diseases by lurid pictures of what may happen to him, such as G.P.I. or locomotor ataxia, if he acquires venereal disease or by an appeal to avoid exposure because of the possible effects on his future wife and children. The unanimous opinion was that the latter is the more fruitful approach.

#### SMALLPOX

To change the subject, a reminiscence of January 1919 may interest you. I was asked by a Bootle doctor to see a man with what he said was a peculiar rash. The man opened the door himself. He said he was well but he was covered with the most profuse rash I had ever seen. It was a characteristic smallpox rash which he told me had appeared three days before. In my previous experience of smallpox anyone with a quarter of that rash would have been prostrate and very ill. However, I sent him into hospital as a case of smallpox and made further investigation. A fortnight before his rash came out, he had gone to meet his brother who was a stoker on a ship sailing to and from Lisbon. His brother told him that on Christmas Day, 1918, while they were at sea he had, after a few days' illness, come out in a rash. He had shown it to the ship's captain who had told him his blood was out of order due to drink, given him a dose of salts and told him to go back to work. As, on the next day, he felt better he had agreed with the captain's diagnosis. Before they went home from the ship, the two of them had gone to tell the story to their doctor. He was puzzled but he also saw no reason to revise the diagnosis and it was only when the brother developed a rash that his suspicions were aroused and he consulted me. To cut a long story short: The stoker had probably contracted variola minor, as we subsequently called it, in a drinking den in Lisbon where smallpox was reported to be present in the Local Government Board's weekly circular. True to form, he had visited dozens of public houses in Liverpool and Bootle and we could not trace more than a small proportion of the contacts. The occupation of the man I first saw was to scrape ships' bottoms. The day before I saw him he had attended with 100 other men to receive his pay. All were kept under surveillance but none contracted smallpox. The wife and the two children of the stoker developed smallpox and, apart from the brother who first came to notice, there was only one other case. This was a curious occurrence. He was a middle-aged man who lived some miles away from the small nest of discovered cases. He gave his occupation as a timber clerk and no contact with the other five cases could be elicited. We thought there was an undiscovered case linking him with the others and that we were in for trouble. Quite unexpectedly the mystery was solved. In casual conversation with the ward sister at the smallpox hospital he mentioned that he had a friend who worked at a cinema and sometimes he took an evening's duty for him. In the history of the two children with smallpox was a statement to the effect that they had gone to the pictures the night before the rash came out. On that very night patient No. 6 had relieved his friend and one of the children had evidently handed him smallpox along with the metal admission tally. This was in the vestibule. The children had sat with scores of others in an ill-ventilated cinema, adapted from a theatre, and did not infect anyone inside. To the best of my knowledge this was the first appearance in this country of variola minor, which later became so prevalent.

While on the subject of smallpox, two other incidents may be worthy of record. In those days the Medical Officer of Health of a small town acted as the general consulting physician for those who could not afford to pay a private consultant. A few months after the occurrences just recorded, I was asked to see a man, in a humble habitation, who had suddenly become unconscious the previous day. He was very ill, breathing stertorously and his back was slate-blue. There were similar blue patches on his limbs and on the strength of a few pustules on his face I sent him into the smallpox hospital as a case of suspected hæmorrhagic smallpox despite the fact that there was no smallpox in the country at the time. In fact, the origin of the outbreak was never discovered. My diagnosis was confirmed by Dr. C. O. Stallybrass. I employed American methods of mass publicity to get those living in the neighbourhood vaccinated, including attendance in the street where the man lived, and from the crowded tenements they poured out in hundreds and were vaccinated there and then in

warehouses were examined and one of them also was found to be plague-infected. Enquiry from the Port Authority then revealed that the only cargo common to the two warehouses where the plague-infected rats had been found was Egyptian cotton received a month or so before. On arrival in Liverpool part of the cargo of cotton had gone to the Bootle warehouse, part to that in Liverpool. There was plague in Egypt at the time. But the story is not yet finished. About three weeks later, a boy was sent into the Liverpool Royal Infirmary with symptoms pointing to appendicitis. On exploration, the appendix was found to be normal but the very careful surgeon—Mr. (later Sir Robert) Kelly—noticed that some of the adjoining glands were enlarged and inflamed. He cut one out and sent it to the laboratory. The next day was Whit-Monday and the Association of Physicians was meeting in Liverpool. The Assistant Pathologist, later a distinguished member of the Public Health Service, called in hurriedly on his way to the meeting to deal with anything really urgent. He did not regard an inflamed abdominal gland as coming within that category but the technician had made a smear from it so the pathologist looked at it and found it contained typical *B. pestis*. He did not get to the meeting! The boy was found to come from a flea-infested house, his father had died suddenly of what was certified as "pneumonia" a fortnight before and he had worked at a paint factory which was next door to the warehouse where the Liverpool plague rat had been discovered. Fortunately there were no further cases, so far as is known, among rats or men.

To revert to my publications, the increasing interest of the public health service in the personal health services is evident. In 1911 I wrote a report on Tuberculosis and Tuberculin Dispensaries following a visit to London where I saw the work done by Drs. R. S. Walker, Halliday G. Sutherland and W. Camac Wilkinson, the last with at least one duchess watching him give injections of tuberculin.

#### HOME HELPS

In 1920 I wrote a paper on Home Helps [2]. I had selected a few women, sent them for three months' experience in a residential nursery so that they might learn how to look after a very young baby, and offered their services to Bootle mothers during their confinements. Almost with one accord, the mothers, who, when asked, had said how much they would like help at this period, having seen the proffered home help, began to make excuses and thought they could manage. I had chosen the home helps because they were smart, good-looking women and enquiry showed that the mothers would have been glad to have them about the house if they were plain, or preferably, positively ugly, or if their husbands had been at sea or for some reason not at home. The few who were acceptable to the mothers fell out with the midwives because they were for ever telling them how differently, and better, babies were looked after in the places where they had been "trained". It was not until I was in Hull some years later that I had the courage to start another Home Help scheme. I profited by my experience. They were given no training in child care and the best candidates independent of what they look like.

During the first World War one of my jobs was to act as Medical Officer of the two Liverpool Dock Battalions. I gained an insight into the hazards of dock labouring and wrote a paper [3] on the physique and working capacity of the Liverpool Dock Labourer. The average number absent through injury was 7.7 per 1,000 and through sickness 43.7. I was impressed by the need for decasualizing this form of employment which, I am glad to say, has recently been done.

#### HEALTH EDUCATION

Soon after that war I became interested in the education of the public on how they could help themselves to good health by having imparted to them simple facts about how the body works, the infections and the diseases which assail it, the importance of consulting a doctor in the early stages of illness and the public provision made to safeguard health. This is an interest which remains with me still. I wrote much on the subject, including a book [4], and took an active part in the foundation in 1926 of what is now the Central Council for Health Education. I studied the technique of handbills, most of which at that time were deplorable in their set-out and phraseology, posters, health exhibitions and health lectures. There are three types of medical lecturer. The majority who have the basic knowledge but cannot put it into the simple language which the general public can understand. A small number who have a magnificent presence and delivery but who say things which outrage those doctors who believe that the public should be told only "the truth, the whole truth and nothing but the truth". Then there is the *rara avis* who knows both what to say and how to say it. There was in those Northern towns a remarkable avidity for information on health



cases—at that time practically all cases of scarlet fever were admitted to hospital—and too much on disinfection. Despite the depressing result of my researches I felt that we spent too little on the maternity and child welfare and school medical services and too little on health education. I was still inclined to agree with the Health Commissioner of New York, Dr. Herman M. Biggs, that “Public Health is purchasable”.

Financial stringency in public expenditure is again beginning to appear, though at a somewhat longer interval than after the first World War. I have no doubt that we would profit now also by examining where the money goes and which outlet gives the best return. Within the next year or two we may be forced to consider these problems and justify the expenditure. I am sure we all have ideas on the subject which may be briefly summarized by saying that more and more money is needed to do our own particular work properly as we are handicapped and frustrated at every turn because of lack of staff and money. We add that we really cannot understand why so much money is allotted to—here follows a list of subjects in which the speaker is not interested—where the waste and the lack of results are deplorable. In effect, extravagance is other people's expenditure. But this emotional reaction which does credit to our keenness on our own jobs, though understandable, does not carry us very far and a dispassionate survey is, in my view, essential.

#### ATMOSPHERIC POLLUTION

Blackburn is a smoky town. Like most weaving centres established before artificial humidification was introduced, it is in a hollow surrounded by hills and from the hills, as one looks down on the town, one sees scores of factory chimneys, each in times of prosperity belching forth smoke. I became interested in atmospheric pollution [6]. I demonstrated the effect of smoke on buildings, on the washing and cleaning bill and particularly on infant life. The relationship between fog and the respiratory death-rate is well established and it is a fact that the main difference between rural and urban mortality is in the deaths from respiratory diseases. Much of the information I collected at that time came in useful when, some ten years later, I gave evidence before the Electricity Commissioners on the proposed Fulham Power Station and the importance of steps being taken to prevent or reduce the emission of grit and sulphur gases. I started a campaign to try to effect some improvement in the atmosphere of Blackburn by a stricter application of the sections of the Public Health Act relating to the emission of smoke, by classes for stokers, by popularizing gas and electric heating and by focusing public attention on the importance of the subject. We sent a pressing invitation to Mr. George Bernard Shaw to give a lecture in Blackburn. The answer was on a post card. It was to the effect that he couldn't understand why we should think he could ever be induced to visit Blackburn. If ever he had the misfortune to be there his only thought would be as to how he could escape as quickly as possible. This reply was not well received by the dignitaries of the City! War is a great destroyer of much which has been achieved by hard work and it is regrettable that during the last war factory owners had to be encouraged to allow smoke to pour out of their chimneys in order to help to conceal the towns from raiding aircraft.

#### PLAGUE AGAIN

In 1925 I moved to Hull. It is a most valuable experience to go from town to town but I doubt if those members of our profession who spend their working years in the same locality realize how upsetting these moves are to domestic life. One has to find a house, make new friends, and disturb the education of one's children, quite apart from the heavy expenses incidental to a move of this sort. It is part of the price we pay for membership of the public health service. I was Medical Officer of Health of the Port of Hull and Goole as well as Medical Officer of Health of the City. I soon found myself studying the problem of rat-infestation of ships, the best type of rat-guard to be placed on the hawsers and the other measures to be taken to prevent ship-rats getting ashore. My most exciting experience was when an Italian ship, loaded with grain from Rosario, arrived. She had presented a clean bill of health and, after examination of the crew by the assistant Port Medical Officer of Health, had tied up at the quayside awaiting her turn to discharge the grain into the elevator. The next morning one of the port rat-catchers brought to the laboratory a few dead rats which he had found on the top of the grain. The usual routine examination of a smear from the spleen was made and Dr. Edward G. Clark, my assistant, and I both thought we saw *B. pestis*. We had to take a very serious decision. Were we sufficiently certain, to justify our requiring the ship to be moved to the mooring place for ships in quarantine which would involve the owners in considerable expense and which would, if we proved to be wrong, very probably lead to an action by the owners against the Port Sanitary Authority for the recovery of their losses? We took the risk and the ship, to the indignation of the owners, was moved. A messenger bearing the rat in a well-sealed packet and our slides was despatched to London by the midnight train and we spent anxious hours until, the next afternoon, the Ministry of

the street on that fine summer evening. The dramatic circumstances of his sudden illness, the arrival of the ambulance and the news of his death, for he died a few hours after admission to hospital, no doubt contributed to this. Of the other six occupants of the house where he lived, one only was protected by recent vaccination, all the other five contracted smallpox in a severe form from which one died. There were only two other cases, one a workmate and the other a child who had played with the children from the infected house. The absence of serious spread was doubtless due to the fact that this form of smallpox strikes down its victims suddenly. They must take to bed and nearly all the contacts are house-contacts. Danger arises, however, even in this type of smallpox when the immunity of a vaccinated person is weakening.

The last smallpox story I will tell you was the beginning of the large epidemic of variola minor which occurred in this country between 1922 and 1934 and caused about 70,000 cases but with an exceedingly small mortality. When I was in Blackburn the local Medical Society was short of readers of papers so during the session 1921-22 I gave them one on infectious diseases in which I referred to the differential diagnosis of smallpox. Among those present was Dr. Gilbert Orme, then of Clitheroe, a small town ten miles away. A few weeks later he telephoned to ask me to see a case with him. He thought it might be smallpox but admitted that this possibility would never have occurred to him had he not remembered what I had said about this disease at the medical meeting. I was informed that the patient was a small girl who had arrived from Canada two or three weeks before, together with her father and mother, on a visit to her grandparents in Clitheroe. A week before I saw her she had had "influenza" and then had come out in a few spots for which Dr. Orme had been consulted. When we got there we found that the patient had gone, with one of her cousins, to a school where a concert was giving an entertainment. We extracted the child from a group of about 40 children, all packed closely together, watching the performance. The rash was scanty but had the typical rounded pustules of smallpox and the distribution fitted that diagnosis. I will never forget the abuse I received from the grandfather, aged 72, when I said the child must be taken to the smallpox hospital. The family had come from Canada in a ship named the *Montcalm* and I discovered that a case of "chicken-pox" had occurred during the voyage. The grandfather (previous vaccination seventy-one years before) developed smallpox himself a few days later and apologized for his abuse. I did not see the mother as she and her husband were visiting a sister in Nelson and I have little doubt that the girl was the cause of the Nelson and Colne outbreak which started very shortly afterwards and which spread throughout the country.

#### INFLUENZA

Reverting to 1918-19, I have vivid recollections of the devastating epidemic of influenza. The death-rate shot up to unprecedented heights and affected mainly those under 45. The Health Authorities were really powerless to prevent its spread. Writing at the time I said: "It is probable that the mental depression caused by the War, the shortage of food, overcrowding consequent on lack of sufficient housing accommodation and the overcrowding of persons in single rooms owing to shortage of fuel, all played their part in causing the rapid spread of the disease once it had been introduced into the country." All these conditions have been present again before and since the end of the last war and I surmise that it is only because a virulent form of influenza has not been introduced that we have escaped a similar visitation.

#### COSTING

In 1921 the Geddes Axe had struck and all public expenditure was subjected to close scrutiny. I wrote several papers [5] analysing the allocation of the costs of a public health improved health and reduced mortality. This self-examination was in some respects a salutary and even mortifying experience and it is an exercise which might well be resumed. I discovered that in County Boroughs the expenditure of public health departments varied from 2s. 3d. to 9s. 4d. per head of the population and from 34d. to 2s. 6d. in the pound of rateable value. I examined the vital statistics of towns which appeared to be similar in housing and social conditions but where the expenditure on public health services differed widely, for example, the mortality of infants or from tuberculosis. At that time, of every £100 spent by the Health Departments of County Boroughs £26 were spent on work against infectious diseases and £30 on anti-tuberculosis work, mostly, in both cases, on hospital (or sanatorium) maintenance, £13 on maternity and child welfare, £9 on the school medical service, £5 on the venereal disease scheme, £2 on food and milk control and £15 on general sanitary work and administration. I then asked myself the questions: "Is that the proper distribution of the money?" and "In what branches of our work should we expect to get the best returns?" I came to the conclusion that we were spending too much on the hospitalization of fever

with a view to becoming a physician, and subsequent experience, had proved invaluable. All that I left behind and I became an office doctor—still attending and taking pleasure in clinical meetings but no longer having responsibility for the diagnosis or treatment of any individual sick person. While the London County Council remained a great hospital service, it gave me great satisfaction to know that I could still serve the sick. I visited the hospitals constantly to talk to the doctors and the nurses and find out what was needed to enable them to give better care to the sick. I regarded it as the primary duty of the medical administrator to provide the tools—the staff, the equipment, the buildings—by which better care could be given to the sick. Until the war, we were reasonably successful in doing this. But, overshadowing all, I had a deep-rooted adherence to the importance of preventive medicine. Access to the hospitals, to their records of the conditions for which people sought treatment, and to the doctors who talked about their "cases", gave information which was invaluable in deciding what was needed to improve the health of the community, what were the illnesses which were most important from the public health and preventive or social medicine points of view, which diseases were preventable, either absolutely or relatively, by getting them under treatment earlier and so preventing more serious illness, what better provision for treatment should be made and what were the failures and deficiencies of the service. I liked planning and had ample scope for such talents as I possessed. As a result of the passing of the Local Government Act of 1929, much reorganization was needed. Seventy-six hospitals were transferred from the Metropolitan Asylums Board and the twenty-five Boards of Guardians to the administration of the Public Health Department. Subsequently twenty-two mental hospitals were added to the responsibilities of the Department and the ninety-eight hospitals contained 72,000 beds. In addition to this, there was the pre-1929 Health Department with a large range of activities including the school medical service, the tuberculosis service, the scheme for the control and treatment of venereal diseases, slum clearance, registration of nursing homes, certification of the blind, ascertainment of the mentally defective, advice on sewage disposal and a host of other things. I was fortunate in my chief, Sir Frederick Menzies, who gave me a free hand, and whom I succeeded in 1939, and in my colleagues, Drs. W. Brander and J. A. H. Brincker. We were very much like the Managing Directors of a big business. The Council and its Committees were the representatives of the Shareholders, the ratepayers of London, and corresponded to the Board of Directors. The staff numbered finally 40,000 and the annual expenditure exceeded £15,000,000.

In our reorganization we tackled first the tuberculosis scheme and with such success that until two or three years ago the waiting period for institutional treatment was between two and three weeks only, and for urgent cases there was no waiting period at all. Then we reorganized the district medical service and ensured that all the destitute sick had the immediate services of a doctor and, if a hospital bed were needed, he got it forthwith. It is interesting to reflect that now when everyone is entitled to a free doctor and free hospital treatment, the destitute who were the special care of local authorities and had priority rights have lost their privileged position and if there is a queue for medical care they take their place in it. We found that the facilities for clinical pathology in the hospitals transferred from the Boards of Guardians were poor and, in some, almost non-existent. A small committee of which I was Chairman, and greatly helped by Dr. Brincker and Dr. J. McCartney, worked out a scheme for *Group Laboratories* which were soon provided and ensured that the more urgent examinations could be made for every patient. It laid the foundation of a really sound and efficient service and the Council was most fortunate in the Group Pathologists who joined its staff.

#### RESEARCH

Another important Committee, of which I was Chairman, reorganized the ambulance service, making two divisions—the accident service and the removals service. But perhaps the most important Committee of all was the Hospital Standards Committee. This included in its membership not only medical superintendents but also architects and engineers. We were really a study circle. We acquired all the information obtainable about everything connected with hospital work. Staff, equipment and buildings were studied. We reported at length on the relative merits of vertical and horizontal construction. We planned a new type of ward, went closely into the innumerable details of the construction and equipment of sluice rooms, operating theatres, radiological units, out-patient departments, hospital kitchens, laundries, nurses' homes, &c. &c. Our reports were as big as some books. There is much basic information in them which had never been gathered together before and as they are no longer of any value to my department I have given them to the Hospital Information Bureau of the King Edward Fund. Two other Committees of great interest and value must be mentioned—the Clinical Research Committee and the Mental Health Services Research Committee. There was cross-representation between the two. The Committees were appointed for the purpose of encouraging research in the Council's hospitals and of

Health's laboratory telephoned to say, with the usual caution of a Government Department, that the microscopic examination appeared to show *B. pestis* but they couldn't be sure until the result of cultures, which they had taken, was known. In due course, we were told that the culture was positive. In the waiting period we had worked out what we would do. We took the crew to the isolation house attached to the disinfecting station and stoved their clothes. We disinfected the ship with cyanide—which was then a fairly new method and, as we knew, fraught with danger. Then the crew returned and we required the grain to be run in a slow trickle down chutes into a barge alongside. We had men posted to make sure no rat, dead or alive, went out with the grain. When all was discharged we found a large number of dead rats in the holds. We suspected there were still a few live ones so we fumigated the ship again before releasing her and giving a deratization certificate. Fortunately throughout all this period the crew remained well and there were no passengers. The cost to the owners of the delay and the expensive method of discharging the grain must have been enormous. One wonders if anything serious really would have happened if we had failed to spot the organism in the spleen smear. I could not help pondering over the responsibilities carried by, at least in my case, so-called experts when I was recently crossing to New York. The ship's surgeons were worried about a woman in the tourist class who had developed what one of them thought was chicken-pox and the other smallpox so I was asked if I would arbitrate. I was fairly certain it was chicken-pox and gave a certificate, quite as a work of supererogation, that it was. It turned out that I was right. But if I had played for safety and certified that it was even suspected smallpox the delay and fuss on arrival in America would have cost the Steamship Company many thousands of dollars, quite apart from frayed tempers and righteous indignation against the "fool of a doctor".

Even the most experienced can make mistakes. I remember a Lascar whose rash was demonstrated to a class of students, by the author of a book on the diagnosis of smallpox, as showing the characteristics of chicken-pox. A fortnight after his admission, a contact developed typical smallpox.

Reverting to my work as Port Medical Officer of Health, ships from the Far East and from infected ports had to be boarded before they came alongside the quay. We were lucky if we could get aboard while they were passing through a lock. Often we had to board in midstream and undertake the perilous task of climbing a rope ladder up what appeared to be the mountainous side of a swaying ship. I learnt a useful tip from an old sea captain. In ships from plague-infected ports we examined the groin for enlarged and painful glands. This was embarrassing to female passengers and they resented it. The tip he gave me was to put a rope across the gangway along which they had to walk to the examination cabin. The rope was about eighteen inches from the floor. If the flexion of the thighs needed to negotiate this caused no discomfort there was no occasion to concern ourselves about painful inguinal glands. We derived some amusement from watching obese passengers tackle this obstacle.

#### POLIOMYELITIS

In 1927, when I was on the Continent with my family enjoying what I thought was a well-earned holiday, I was summoned back to Hull to cope with an epidemic of poliomyelitis. Up to then the average number of notifications in Hull had been, over many years, 1.5 per annum. During August and September there were 110 cases. It is a most curious disease. It had been rumbling in the Isle of Thanet for two or three years. Leicester had had a sharp outbreak in 1926 and Glasgow had one in 1928. In 1926, 1927 and 1928 there were the usual odd sporadic cases throughout the country but I could never explain why Leicester alone, Hull alone and Glasgow alone were singled out for epidemic spread in those successive years. In a paper read before the Hull Medical Society I suggested that when a town is attacked by an epidemic the infection is very widespread but that very few go on to the paralytic stage. Experience during the widespread outbreak of 1947 tends to confirm that view and, in fact, it is now, I think, established that there are about 200 infections or latent cases for every clinical case.

#### ADMINISTRATIVE WORK

In 1929 I came to the County Hall of London. It opened up many new spheres of activity but I left the provinces with very real regret. Though I had had much organizational and administrative work to do I had always regarded myself as a "proper doctor". I had endeavoured to retain clinical skill. I occasionally took a child welfare clinic, a session at the Tuberculosis Dispensary, I was the Medical Superintendent of the Corporation Hospitals and saw patients there regularly. I was frequently called in consultation by general practitioners, particularly for the infectious diseases, and as they included infections of the central nervous system such as encephalitis lethargica and the differential diagnosis covered a wide range, my early training

County Councils from district councils and by the abolition of the Boards of Guardians. The process of transfer to even larger units of administration goes on; this time from Local to Central Government, for example, the eradication of tuberculosis in cattle to the Ministry of Agriculture and the Hospitals to the Ministry of Health, working through Regional Hospital Boards and Boards of Governors of Teaching Hospitals. Even within local government there are transfers away from public health departments, e.g. to new Children's Departments. On the other hand, Local Government as a whole is still very strong and I cannot agree with those who suggest that Medical Officers of Health should become State officers. Their work in the environmental health services and in the school health services is too inextricably mixed with duties which must remain in the field of Local Government for any separation to be possible without lessening materially the efficiency of the service. There is, however, no doubt that certain units of Local Government are too small and a complete reorganization is overdue. The last report of the Boundary Commissioners gives a clue as to the shape of things to come.

I notice that many of the papers I have written lately have been surveys of the historical background of the health and hospital services of London or of the country [8]. I have always held that if we wish to know why things are done in a certain way we must know why they originated and how they developed. In this country we are not ruthless revolutionaries. We never rub out all the writing on the blackboard and start again. Sometimes I have wished that we did. But we adapt and use as much of the old machinery as we possibly can. That is why the administrator who has a passion for "tidiness" is generally not a great success. There probably never was a more complex administrative system than exists to-day in our health and hospital services. There is no "London Hospital Service". There are thirty separate hospital administrations in the metropolis even when we count the four Metropolitan Regional Hospital Boards each as one and disregard the thirty or so Hospital Management Groups. I have written much to demonstrate the close link there must be between the public health and the hospital sides. This runs through the maternity services, the child health services, epidemiology, the tuberculosis and the venereal disease services and the mental health services. The relationship between the county health services and those of the sanitary authorities—the municipal and metropolitan boroughs and the urban and rural districts—needs to be clarified. It is quite clear that my last few years of official life will have to be spent in trying to devise an arrangement by which the various pieces of the jig-saw puzzle fit together and that there are no gaps and no pieces left over. This brings me to the subject of Committees. When there is unified administration there is always someone who, in the last resort, can give an order with the reasonable expectation that it will be carried out. If he is a sensible administrator, he consults a few of his principal colleagues and obtains their views before he issues it. But this doesn't take long and, if need be, decisions can be taken and acted upon within a few hours. But when administrations are separate and independent, everyone is sensitive about his dignity and develops a loyalty to his own administration, coupled, it would appear, particularly in the lower ranks, with a distaste for, and suspicion of, other administrative bodies and their officers. There are formalities to be gone through even before a meeting can be summoned. Then the meeting is held. Difficulties, real or imaginary, are raised and, as often as not, no firm decision is reached and so further meetings are needed. It is impossible to get drive and effectiveness unless one person is in a position to keep nagging away to ensure that everyone realizes the importance of the particular task in hand.

To-day we spend so much time in committees that inadequate time is left for quiet thought. It is a human weakness that anyone in a position of authority insists that he must be consulted on any and every matter in which he is, even remotely, concerned and if he isn't consulted he is obstructive. With so many now having positions of authority the number of Committees concerned with, for example, the public health services of London is countless. It is, I suppose, part of the price we pay for democracy.

#### THE WAR 1939-1945

The title of this Address is "I Remember" and it is perhaps strange that I have almost reached the end without a single reference to what I remember most vividly, namely the recent war. It is perhaps a failing of the old that their thoughts dwell too much on the distant past rather than on the recent past, the present and the future. We had done a lot of preparatory work before war broke out. When it did, my three main tasks were to keep the municipal hospital service going, to expand and administer the ambulance service and to deal with the medical problems arising from the evacuation scheme for London mothers and children. I moved into County Hall and slept, until I was bombed out, in my office and after that in a cellar. It certainly was exciting, though somewhat of a nightmare. Reports of hospitals being hit were constantly being received by telephone or messenger—generally in the middle of the night. Hospitals had to be evacuated at short notice and casualties

helping any research worker who sought their advice or who needed special equipment or other assistance. They were appointed on a democratic basis and the members served for limited periods in order to ensure that new blood was regularly introduced. Sometimes we originated enquiries and asked for volunteers from the hospitals to undertake the necessary investigations. The records were handled centrally under expert statistical advice. One of these researches was on the after-history of pleurisy, another on the viability of strangulated gut. It is only in a large organization that researches of this kind can be carried out. The variety and quantity of clinical material were unsurpassed and the records were kept in such a form that a summary card giving the essential particulars of all patients admitted to the Council's hospitals was sent to County Hall. There, by punched cards and mechanical tabulation, any information needed by a research worker could be obtained. If anyone wished to look up the actual case papers of patients suffering from some rare disease, the cards of some thousands of admissions could be put through the machine and within a few minutes he could be told the hospitals where the patients were treated and the reference numbers of the case papers. Unfortunately with the break-up of the L.C.C. hospital service these Committees have been disbanded. I hope that something will arise to take their places.

#### SCHOOL HEALTH SERVICE

One of my special responsibilities during my first ten years at County Hall was the School Medical Service. I was impressed by its magnitude and its high quality especially in the provision of special schools of every variety. I read a paper on "School Life and After for the Handicapped Child" before this Section in April 1938 [7]. There are two unique features in the London School Health Service. The first is the large use made of part-time doctors. Many, perhaps I should say most, of the paediatricians of London and many ophthalmic and aural surgeons have, at some time or other, worked in the London School Service. Dr. C. J. Thomas acted as their mentor and took great pleasure in reciting their names and subsequent distinctions. The other unique feature is its child-care organization in which trained social workers, assisted by voluntary care committee members play an important part in promoting the welfare of the children, particularly perhaps by helping the parents to obtain any treatment which is advised.

#### MEDICAL EDUCATION

During recent years I have taken increasing interest in medical education, particularly post-graduate medical education, and have the privilege of being a member of the Board of Governors of the British Post-graduate Medical Federation and of the Committee of Management of several of the constituent Institutes. This interest started because of my responsibilities for the administration of the L.C.C. Hammersmith Hospital to which, in 1935, the British Post-graduate Medical School (now the Post-graduate Medical School of London) was attached. The L.C.C.'s Maudsley Hospital had been a school of the University for the training of psychiatrists since 1924 but the Council had borne the cost of the School. The use of Hammersmith Hospital by the Post-graduate School, the cost of the teaching being met by the University, was the first time in this country that a university teaching institution financed by Government money had not been based on a voluntary hospital. It was, however, almost stillborn. A post-graduate committee had been formed, all the necessary consents from the University, the Treasury and the L.C.C. had been obtained, when the financial crisis of 1931 suddenly enveloped us. The agreement had been that the Treasury and the L.C.C. should each find £250,000 for new buildings and equipment. These sums would provide the necessary buildings for the school and would provide new wards for the enlargement of the hospital. The fiat came that the Treasury money was no longer available and the scheme on which many years of hard work had been spent seemed dead. Lord Chelmsford, the Chairman of the School Committee, and I saw the then Permanent Secretary of the Ministry of Health and explained what a disaster it would be if the scheme were abandoned. Sir Frederick Menzies, who was then on leave, returned to London shortly afterwards and reinforced this with the final result that the scheme could proceed but the Treasury grant was cut to half. The L.C.C. did the same, with the result that the school has been crippled by the inadequacy of its buildings ever since. It is a great tribute to all concerned, particularly the professorial staff that, despite these handicaps, the school can claim such magnificent achievements and is now known throughout the Empire and Dominions and indeed the world.

#### LOCAL GOVERNMENT

During the past twenty years my main interests, as shown by my writings and lectures, have been administrative. I have given much time and thought to the organization of local government. I have seen the gradual building up of the powers and duties of the Health Departments of the Counties and County Boroughs by new duties, by transfers of duties to

## Section of Anæsthetics

President—RONALD JARMAN, D.S.C., F.F.A. R.C.S.

[April 1, 1949]

### ANÆSTHETIC RESPONSIBILITY

**Mr. W. R. H. Heddy** (*His Majesty's Coroner for East London*):

In strict law what is the duty of the anæsthetist towards his patient?

The answer that would be generally given, I suppose, would be that it is his duty to take care.

And that answer, though it would not be complete, would not be wrong.

Let us see, then, first of all, why this answer, so far as it goes, would be a right one.

It would be right in the first place because in law such a duty in this case does, in fact, exist.

How and why does this duty exist?

There is in law no general obligation cast upon everyone to exercise care to everyone else in any and every circumstance.

There is, so to speak, no universal compulsion to take care.

As Lord Esher, Master of the Rolls, remarked in the case of *Lelievre v. Gould*: "A man may be as negligent as he pleases towards the whole world unless he owes them a duty."

In other words no action for damages based on negligence can be sustained unless it can be shown that the defendant in law *owed a duty* to the plaintiff to take care.

Such a duty exists in law in a vast number of personal relationships.

The case of doctor and patient is one of such relationships.

And in the case of medical man and patient this duty arises from the fact that a duly qualified medical man holds himself out as having special qualifications that imply the possession of some special knowledge and skill.

The mere fact that he is a doctor immediately creates this legal duty to exercise care towards his patient.

attended to. The total number of "incidents" such as the bursting of high explosive bombs or a rain of incendiary bombs, which affected the L.C.C. hospitals was 660. The number of beds totally destroyed was 4,456. On eighteen occasions a hospital had to be totally evacuated—in one case this involved the removal of some 2,000 mental patients. On many occasions bombs fell on County Hall and I was bombed out of three offices but despite physical discomforts we kept going. No acute case of illness and no casualty ever failed to get a bed in an L.C.C. hospital. For this I must pay a tribute to the magnificent work and gallantry of the hospital staffs. They never flinched even during the grimmest and darkest days of the war. It was a dangerous occupation to be in London at that time. Many hospital and ambulance staff lost their lives. Many more were injured. Yet, the service never failed and morale was high. I sometimes wonder whether we appreciate sufficiently how much London, and indeed the country, owes to them for their undaunted steadfastness.

Memories still crowd upon me. I think of the hosts of friends I have in all parts of this country and abroad. I think of my mentors in my hospital days, of the early pioneers of public health in this country, many of whom were known to me, of the officers of the Local Government Board and the Ministry of Health and of the Board, and later the Ministry, of Education who have always been so helpful, of my colleagues in public health, in this Section, who have honoured me by making me their President, and in the Society of Medical Officers of Health where they have been equally kind, of the leaders of the Profession in the Royal Colleges, the Society of Apothecaries and the British Medical Association, to whom I have never turned for advice in vain, of the various Chief Officers of other Departments with whom I have always worked with great cordiality, of the members of my own Departments, from whom I have ever had loyal and devoted service, and finally of the members of the Authorities for whom I have worked. My relationship with them has always been the best. As the years roll on I have been more and more impressed by the zeal and devotion to the cause of their fellow-citizens which animates those who serve the public, quite voluntarily, as members of local authorities. They receive little thanks and much abuse. The public health services of this country could never have shown such astounding success as is evident in recent vital statistics if they had not listened to the advice of their medical officers of health and found the necessary cash to implement that advice.

I trust I have not wearied you unduly by this long recital of the things which have interested me. The writing of it has revived many memories of events which were beginning to fade, some of which I hope may also have interested you.

#### REFERENCES

- 1 DALEY, ALLEN (1913) Rats and their extermination, *Publ. Hlth.*, 27, 23.
- 2 — (1920) Home helps and maternity and child welfare, *The Child*, 11, 46.
- 3 — (1921) Observations on the physique and working capacity of the Liverpool dock labourer, *J. Roy. San. Inst.*, 41, 256.
- 4 —, and VINEY, H. (1927) Popular Education in Public Health. London.
- (1924) The organisation of propaganda in the interests of public health, *Publ. Hlth.*, 37, No. 12, 305.
- (1924) Health weeks, *The Hospital and Health Review*, 73, No. 1874, 146.
- 5 — (1921) A review of the costs and results of the various public health activities, *The Medical Officer*, 26, No. 4, 39.
- (1922) The economics of child welfare—child welfare work, *National Health*, 14, 111.
- 6 — (1922) Atmospheric pollution and health, *Bull. Brit. Comm. Gas Ass.*, 11, No. 109, 66.
- 7 — (1938) School life and after for the handicapped child, *Proc. R. Soc. Med.*, 31, 1013.
- 8 — (1948) The health and municipal hospital services of London, *Brit. Med. J.* (ii), 19.
- (1948) The health officer in post-war Britain, *J. Amer. Publ. Hlth. Ass.*, 38, No. 3, 325.
- , and COLEMAN, R. (1942) The development of hospital services with particular reference to the municipal hospital system of London, *Proc. R. Soc. Med.*, 35, 741.



## Section of Anæsthetics

President—RONALD JARMAN, D.S.C., F.F.A. R.C.S.

[April 1, 1949]

### ANÆSTHETIC RESPONSIBILITY

**Mr. W. R. H. Heddy** (*His Majesty's Coroner for East London*):

In strict law what is the duty of the anæsthetist towards his patient?

The answer that would be generally given, I suppose, would be that it is his duty to take care.

And that answer, though it would not be complete, would not be wrong.

Let us see, then, first of all, why this answer, so far as it goes, would be a right one.

It would be right in the first place because in law such a duty in this case does, in fact, exist.

How and why does this duty exist?

There is in law no general obligation cast upon everyone to exercise care to everyone else in any and every circumstance.

There is, so to speak, no universal compulsion to take care.

As Lord Esher, Master of the Rolls, remarked in the case of *Lelievre v. Gould*: "A man may be as negligent as he pleases towards the whole world unless he owes them a duty."

In other words no action for damages based on negligence can be sustained unless it can be shown that the defendant in law *owed a duty* to the plaintiff to take care.

Such a duty exists in law in a vast number of personal relationships.

The case of doctor and patient is one of such relationships.

And in the case of medical man and patient this duty arises from the fact that a duly qualified medical man holds himself out as having special qualifications that imply the possession of some special knowledge and skill.

The mere fact that he is a doctor immediately creates this legal duty to exercise care towards his patient.

As was said in *Seare v. Prentice* in 1807: "He who undertakes the public practice of any profession undertakes that he has the ordinary skill and knowledge necessary to perform his duty towards those resorting to him in that character."

That, then, is *how* and *why* this duty to take care, this duty not to be negligent, exists in the case of doctor and patient.

And this duty, be it noted, does not cease to exist because there is no *contract* between doctor and patient. "The legal wrong is the incompetent or negligent treatment: whether service is remunerated or gratuitous is immaterial" remarked Heath J., in *Shiells v. Blackburne* in 1789.

Not only need there be no contract: the service need not even have been rendered for reward.

The duty to take care is a simple and enduring result of the doctor-patient relationship.

We have, then, this perfectly clear and absolute duty to take care—not to be negligent.

And this brings us to another question.

What is this negligence which, as we have seen, it is the medical man's duty to avoid. For the moment we may define it as carelessness.

Carelessness may vary enormously in degree. It may be hardly noticeable, it may be appreciable; it may be considerable; it may be pronounced; it may be heinous.

In law these degrees of carelessness are unimportant, and are not, in fact, recognized until you arrive at the ultimate state of carelessness.

And that degree of carelessness which you may attempt to define by the use of such adjectives as "gross", "wicked", "culpable", "heinous"—that, and that alone—can be sufficient in the case of death to constitute what is technically known as criminal negligence—a crime—and a crime amounting to manslaughter.

Carelessness of such an exceedingly high degree as this goes beyond a mere matter of compensation between private individuals and becomes a violation of obligations to the State, which can only be remitted by the State.

It is a crime and not a matter for civil proceedings. Carelessness of all lesser degrees than this is never a crime, can be no more than civil negligence which may entitle the plaintiff to damages in a civil action.

I need not waste time in trying to envisage circumstances in which an anæsthetist might find himself faced with a charge of criminal negligence. Nowadays the amount it has to amount "almost to an intention not to take care." I am thinking at the moment in terms of traffic fatalities.

I suppose there are circumstances in which an anæsthetist giving an anæsthetic might be so charged—but I propose to leave such circumstances to your imaginations rather than to attempt to suggest them.

The leading case on the subject, so far as medical practice is concerned—it had nothing to do with anæsthetics—is *Rex v. Bateman*. It is interesting because it shows what an inordinate degree of negligence is necessary to constitute the crime of criminal negligence.

Let us return, then, to all those lesser degrees of negligence which we call civil, or actionable, negligence.

What are the principles which are invoked in law to decide whether, in any given case, negligence may, or may not, exist?

They are principles of comparison. The standards of professional skill required are those of the ordinary and average practitioners in the branch to which the defendant professes himself to belong.

The evidence of such a practitioner is admissible to show that the treatment was up to standard.

But a specialist, such as a professional anæsthetist, might well be liable for negligence in respect of treatment which in a junior, or non-specialist, would pass muster.

The duty of a specialist is referable to a higher test than that of an ordinary practitioner. In *Feeney v. Spaulding* in 1896 it was stated "The duty of a specialist must be referable to such a higher test. Special profession involves higher duty, and the standard to be attained is that of the specialist amongst medical men and not that of the general practitioner."

Liability in cases of established civil negligence extends to the amount of harm actually done, to the amount of damage actually incurred—irrespective of the degree of negligence perpetrated.

Liability to conviction in a criminal case depends, as we have seen, on the degree of negligence.

Hence the saying that what matters in civil negligence is the amount of harm you do; what matters in criminal negligence is how negligent you were.

An action for damages based on civil negligence is a trial of issues between two parties.

An indictment for criminal negligence is a trial of issues between the Crown and one of its subjects in a criminal court.

Both of these proceedings are trials of issues, which are decided by a consideration of facts revealed in evidence.

I have emphasized the fact that a trial of issues is involved in both these instances in order to bring into relief the sharp distinction that exists between these proceedings and the proceedings in the Coroners' Courts.

Here there is no trial of issues; there are no "parties" to the proceedings in a strict sense. The function of this court is limited and highly specialized. It is properly described as a "Court of special jurisdiction". Its function is to find out how, where and by what means a deceased person came by his death.

The court has no authority of any kind to decide issues of civil negligence: its verdicts cannot be so framed.

But in the course of its proceedings to determine how, where and by what means a deceased person came by his death it will of course be traversing facts which will largely be the same facts that may figure later on in a civil court in an action arising in connexion with the death of the deceased.

The facts used may be the same facts, but they will be used for different purposes by the two courts—in the Coroner's Court to reveal how the cause of death arose—in the Civil Court to decide questions of possible civil negligence arising in connexion with the death.

A great deal of misunderstanding exists in this connexion, and I want, if I can, to make the position perfectly clear.

Here is a simple illustration:

A bag of sugar falls from a crane on my head while I am working at the docks and kills me.

The reasons for the fall of that bag of sugar will be an important matter for the coroner who is enquiring into the manner in which I came to my death.

He is bound to enquire into it.

If he does not do so my executors or my relatives may approach the Attorney-General and ask him to have the case reviewed by a Divisional Court with the object of getting the inquisition quashed for "insufficiency of enquiry". The coroner is thus bound to enquire into the relevant facts.

The reasons for the fall of that bag of sugar will be an equally important subject for enquiry in the Civil Court in which my executors or relatives are seeking damages for negligence against somebody in connexion with my death.

The same facts will properly be dealt with in each court.

But the findings resulting from these facts will be used for different purposes by the two courts. In the Coroner's Court they will enable the appropriate verdict to be returned—a verdict which will take no account of whether civil negligence exists or not.

In the Civil Court the findings will enable the court to decide the trial of issues and say whether or not civil negligence has been established.

Since the facts that are important are likely to be the same facts, and since they will probably come to light first in the Coroner's Court, interested parties are likely to be represented there in order that they may hear the evidence and examine witnesses on oath while that evidence is still fresh in their minds. Copies of the depositions or notes of evidence will probably be asked for and will be supplied in order that interested parties may clear the decks and concentrate on the main issues before the action for civil negligence comes on later in the Civil Court.

A jury may add a rider to their verdict. This rider, unlike the verdict, need not be accepted by the Coroner who does, occasionally, refuse to accept it.

I think I ought at this point to mention that while the Coroner's Court has no authority at all in the determination of civil negligence, it has, of course, more than a theoretical interest in the question of criminal negligence.

One of its functions, indeed, is to dispose of the possibility of criminal negligence in all cases of death arising apparently from accident or misadventure, before the verdict is returned. People can be, and occasionally are, committed from these courts for trial at the assizes or the Central Criminal Court.

There are a few special aspects of the anæsthetist's responsibilities to which I should like to refer.

In a sense his position is rather a difficult and unusual one. In the first place he will ordinarily see very little of his patient beforehand. In this connexion it must be remembered that the consent of the patient, if obtainable, or that of his relatives or friends should be obtained before he is given an anæsthetic. Any administration—any form of medical or surgical treatment—any examination of a patient, even, should never be undertaken if there is the slightest suggestion that he may object. In law, such consent may be implied, and this no doubt would be the case where consent to operative surgical treatment has already been granted. Nevertheless, it is desirable that those about the patient should, at least, be given some idea of the nature of the risk involved, if in fact there are grounds for thinking that the risk may be considerable. And in this connexion, as events show, reliance cannot always be placed on other members of a hospital staff. Experience shows that they occasionally do not bring matters such as this to the notice of relatives—and their failure to do so may sometimes let the anæsthetist down very badly.

Then again the position of the anæsthetist is rendered difficult by the fact that he

carries out his duties in association with others. The independence of the anæsthetist is to-day so well established that he is probably perfectly capable of looking after himself in this respect. Nevertheless, he should remember that his is the responsibility for the effects of his administration, and he should not hesitate to make his opinion felt if there are aspects of the joint procedure which is being undertaken which appear to him not in the best interests of the patient from his point of view.

I think also that to-day his duty would include the proper instruction of those specially charged to look after the patient after the operation, in so far as matters concerned with the administration of the anæsthetic come into the picture.

I want to say just a word in conclusion about the Coroner's approach to deaths apparently due to surgical procedure. These cases are from his point of view merely one variety of the deaths which may result from, or be accelerated by, therapeutic measures undertaken in the interests of the patient.

If there seems some reason to believe that death has, in fact, been caused or accelerated by surgical or anæsthetic procedure it becomes his duty to inquire into the matter. Aided by the findings of his pathologist and assisted by the evidence of those present at the operation he will try to discover in the first place whether death, for example, is likely to have come about as the result of surgical shock or whether the case really seems to be due to the effects of an anæsthetic. Even to get thus far with any certainty is by no means always easy. We all of us, in our several spheres, realize how difficult these cases may be. From the Coroner's point of view it is, of course, a great help if such a distinction can be drawn, if only for the fact that it will settle for him the question as to whether it is worth while calling the anæsthetist or not.

If the case looks like a real anæsthetic death the evidence of the anæsthetist will, of course, be of the greatest value. Not only will he be able, perhaps, to throw as much light on the case as anyone else, but the mere fact that he is present in court giving his expert opinion and voicing conclusions arrived at as the result of long and special experience has a most pronounced effect in reassuring the relatives and resolving their doubts and uncertainties. I can assure this audience that this sort of testimony is of real service in this respect. Time and again one finds that people who have come to court resentful and suspicious go away satisfied when they have heard an expert describing what probably happened. I say an expert—and you will understand that from a Coroner's point of view the task of dealing with these cases is immensely easier when, in fact, the administration has been undertaken by a professional anæsthetist.

The responsibility of the anæsthetist will always be a heavy one. The immense advances in the art and science of anæsthetics during the past twenty-five years have, as you so well know, made possible all kinds of surgical undertakings which would never have become possible but for this advance. That means that anæsthetists have cheerfully taken upon themselves added and still heavier responsibilities. Seen from the angle from which I see these things I can truly say that these responsibilities are well and truly shouldered.

**Dr. Keith Simpson** (*Reader in Forensic Medicine, University of London*): Mr. Heddy has discussed the legal responsibilities of the anæsthetist. I propose to confine myself to some remarks about his professional conscience.

At a recent discussion on Anæsthetic Deaths by the Association of Clinical Pathologists Dr. E. H. Rink, anæsthetist to Guy's Hospital, made a remark which must form the foundation of professional—as distinct from legal—responsibility in the administration of anæsthesia. He said: "The giving of an anæsthetic is not merely a matter of mathematical assessment and of technical skill: it is an art." Now no

The reasons for the fall of that bag of sugar will be an important matter for the coroner who is enquiring into the manner in which I came to my death.

He is bound to enquire into it.

If he does not do so my executors or my relatives may approach the Attorney-General and ask him to have the case reviewed by a Divisional Court with the object of getting the inquisition quashed for "insufficiency of enquiry". The coroner is thus bound to enquire into the relevant facts.

The reasons for the fall of that bag of sugar will be an equally important subject for enquiry in the Civil Court in which my executors or relatives are seeking damages for negligence against somebody in connexion with my death.

The same facts will properly be dealt with in each court.

But the findings resulting from these facts will be used for different purposes by the two courts. In the Coroner's Court they will enable the appropriate verdict to be returned—a verdict which will take no account of whether civil negligence exists or not.

In the Civil Court the findings will enable the court to decide the trial of issues and say whether or not civil negligence has been established.

Since the facts that are important are likely to be the same facts, and since they will probably come to light first in the Coroner's Court, interested parties are likely to be represented there in order that they may hear the evidence and examine witnesses on oath while that evidence is still fresh in their minds. Copies of the depositions or notes of evidence will probably be asked for and will be supplied in order that interested parties may clear the decks and concentrate on the main issues before the action for civil negligence comes on later in the Civil Court.

A jury may add a rider to their verdict. This rider, unlike the verdict, need not be accepted by the Coroner who does, occasionally, refuse to accept it.

I think I ought at this point to mention that while the Coroner's Court has no authority at all in the determination of civil negligence, it has, of course, more than a theoretical interest in the question of criminal negligence.

One of its functions, indeed, is to dispose of the possibility of criminal negligence in all cases of death arising apparently from accident or misadventure, before the verdict is returned. People can be, and occasionally are, committed from these courts for trial at the assizes or the Central Criminal Court.

There are a few special aspects of the anaesthetist's responsibilities to which I should like to refer.

In a sense his position is rather a difficult and unusual one. In the first place he will ordinarily see very little of his patient beforehand. In this connexion it must be remembered that the consent of the patient, if obtainable, or that of his relatives or friends should be obtained before he is given an anaesthetic. Any administration—any form of medical or surgical treatment—any examination of a patient, even, should never be undertaken if there is the slightest suggestion that he may object. In law, such consent may be implied, and this no doubt would be the case where consent to operative surgical treatment has already been granted. Nevertheless, it is desirable that those about the patient should, at least, be given some idea of the nature of the risk involved, if in fact there are grounds for thinking that the risk may be considerable. And in this connexion, as events show, reliance cannot always be placed on other members of a hospital staff. Experience shows that they occasionally do not bring matters such as this to the notice of relatives—and their failure to do so may sometimes let the anaesthetist down very badly.

Then again the position of the anaesthetist is rendered difficult by the fact that he

TABLE II.—CAUSES OF DEATH IN 500 CASES

|                                                       | Total | %  |
|-------------------------------------------------------|-------|----|
| Natural causes for which operation is performed ..    | 279   | 56 |
| Operative shock, risks, &c. .. ..                     | 149   | 30 |
| Anæsthetic risks, complications .. ..                 | 40    | 8  |
| Overdosage, bad choice, prolongation of anæsthesia .. | 32    | 6  |

I want, now, to say something of those responsibilities the anæsthetist has which are far more commonly neglected than are due care, vigilance and a reasonable skill in administering the anæsthetic.

No doctor prescribing a dangerous drug fails to record the order for its administration, the date, time and quantity of drug given. If the mode of administration is of significance with regard to its effect, then some careful note on the exact method and timing of administration is germane also. But how often are such records kept? These are simple criteria, hardly more than mere matters of conscience, and there could be no valid excuse for failure to observe them. Of course there are anæsthetists—large numbers of them—who do keep such records, but there are far too many who do not.

Even when some technical data are included it is all too common for them to be casual: I have had to decipher scribbled formulæ for anæsthetics, often clearly inserted after an anæsthetic death, on scores of occasions—when a careful account of the procedure would have gone a long way to illuminate the causation of death, and give some reflection of the interest taken. Slovenly careless work is, I recognize, to be found in any professional circle one cares to examine—but we happen to be considering anæsthetic responsibility to-day. It must not be forgotten that, in the event of a catastrophe, such notes will be subject to the closest scrutiny by many—coroners, counsel, members of courts—who may happen to have the onus of deciding responsibility. Casual records can only reflect badly on a doctor: they are bound to damage his repute—whatever the care he, in fact, displayed in the administration of his duty. Bad notes will belie any plea he may make later as to the exercise of due care at the time, whereas good notes have time and again propped up the doctor who stood in peril, whose skill and care were in question.

It is the anæsthetist's duty to show proper care and a degree of skill commensurate with his station: it is incredibly careless of him not to let the world see that he has, in fact, exercised such care.

Now let us turn to another aspect of the anæsthetist's responsibility. It is plainly his duty to check his apparatus and his drugs, to see that his patient is as far removed as he can ensure from accident and unintentional overdosage. It is plainly also his duty to examine personally his patient in order that he may himself be in a position to assess any physical defect like heart disease or some respiratory disadvantage he may have to take into account. These are matters there is some general agreement upon, but there is another which is more often overlooked. The anæsthetist who is assisting the heroic or enthusiastic surgeon who may have a certain disregard for the responsibilities taken by his anæsthetist in such matters should call a halt as soon as any sign of danger to health arises—not danger to life. Prolongation of an operation for the purpose of teaching has caused death in one case I examined from a well-known London teaching hospital, and in another a period of some months' imbecility from cerebral anoxia preceded death owing to the anæsthetist being "musclcd" out of reach of her subject by visitors who desired to get a closer view of the surgery. It is for the anæsthetist to put a stop to such dangers to his patient: over one and a half hours' teaching on a patient already gravely ill from strangulated femoral hernia constitutes a complete disregard for safety—and for an anæsthetist to find herself sitting on the floor out of reach of her patient because of enthusiasts craning over the patient to see some surgical procedure is almost Gilbertian. Neither

artist can pretend that he is constantly at the height of his artistic potential—sensitive, watchful, alert to slight changes of atmosphere and quick to respond. There are bound to be days when his vigilance is flagging, when he is tired and his skill, though potentially as high as ever, is, in operation, below par: presented with an unexpected emergency he is unready or slow to react, his perception of danger blunted.

These are the moments of real risk to both the reputation of the anaesthetist and to his wretched subject, and if this discussion were to be concerned solely with the experienced specialist anaesthetist I should have little more to say on the subject.

But anaesthetists—like any other professional body—are far from being a standard body of uniform excellence and unimpeachable conscience. Anaesthetists naturally vary in skill and judgment, and in their perception of the responsibilities they shoulder.

TABLE I  
100 DEATHS FROM ANAESTHESIA

| FORM OF ANAESTHESIA      | COC. POIS. | ETHER CONV. | CIRC. FAILURE | CENT. RESP. F. | ANOXIA | COLLAPSE LUNG | OBSTR. AIRWAY | ACCIDENT | BAD JUDGEMENT | No. |
|--------------------------|------------|-------------|---------------|----------------|--------|---------------|---------------|----------|---------------|-----|
| LOCAL                    | 5          | 1           |               |                |        | 3             | 1             |          |               | 10  |
| SPINAL                   |            | 12          |               |                |        |               |               |          |               | 12  |
| INTRAVENOUS              |            |             | 24            | 2              |        |               |               |          |               | 26  |
| RESPIRATORY-GAS & OXYGEN | 0          |             |               |                |        |               |               |          |               |     |
| ETHER                    |            | 10          |               |                |        |               |               |          |               | 10  |
| CHLOROFORM               | 0          |             | 1             |                |        |               |               |          |               | 1   |
| TRILENE                  |            |             |               |                |        |               |               |          |               |     |
| COMPOUND                 |            |             |               | 12             | 8      | 14            | 4             | 3        |               | 41  |
| TOTALS                   | 5          | 10          | 14            | 24             | 14     | 11            | 15            | 4        | 3             | 100 |

Table I reflects several important features of death *due to* as distinct from *associated with* anaesthesia. It would not be unfair to say that those from circulatory failure, respiratory failure, anoxia, pulmonary collapse and obstruction of the airway—85% of the total—with those from accident or mere bad judgment, were preventable.

The most striking individual figure is undoubtedly the 24 deaths from respiratory failure due to intravenous barbiturates: all but 3 of these were due to pentothal, the lethal potency of which had been emphasized by one speaker. The wholesale use of intravenous barbiturates, especially pentothal, lulled many into a false assurance of their harmlessness.

The sooner anaesthetization is, like surgery, paediatrics or ophthalmology, recognized to be an expert procedure demanding serious-minded expert attention the better.

No one can pretend that doctors, given the power in law to administer any kind of anaesthetics, will all respect common sense and reason in recognizing the limits of their skill, but that is what a proper sense of responsibility would demand of them—and what the law expects.

The vast majority of fatalities under anaesthesia are nothing to do with the process (see Table II) and, as this is not a discussion on anaesthetic deaths, I do not wish to enlarge on this aspect.



TABLE II.—CAUSES OF DEATH IN 500 CASES

|                                                        | Total | %  |
|--------------------------------------------------------|-------|----|
| Natural causes for which operation is performed ..     | 279   | 56 |
| Operative shock, risks, &c. . . . .                    | 149   | 30 |
| Anæsthetic risks, complications . . . . .              | 40    | 8  |
| Overdosage, bad choice, prolongation of anæsthesia . . | 32    | 6  |

I want, now, to say something of those responsibilities the anæsthetist has which are far more commonly neglected than are due care, vigilance and a reasonable skill in administering the anæsthetic.

No doctor prescribing a dangerous drug fails to record the order for its administration, the date, time and quantity of drug given. If the mode of administration is of significance with regard to its effect, then some careful note on the exact method and timing of administration is germane also. But how often are such records kept? These are simple criteria, hardly more than mere matters of conscience, and there could be no valid excuse for failure to observe them. Of course there are anæsthetists—large numbers of them—who do keep such records, but there are far too many who do not.

Even when some technical data are included it is all too common for them to be casual: I have had to decipher scribbled formulæ for anæsthetics, often clearly inserted after an anæsthetic death, on scores of occasions—when a careful account of the procedure would have gone a long way to illuminate the causation of death, and give some reflection of the interest taken. Slovenly careless work is, I recognize, to be found in any professional circle one cares to examine—but we happen to be considering anæsthetic responsibility to-day. It must not be forgotten that, in the event of a catastrophe, such notes will be subject to the closest scrutiny by many—coroners, counsel, members of courts—who may happen to have the onus of deciding responsibility. Casual records can only reflect badly on a doctor: they are bound to damage his reputation—whatever the care he, in fact, displayed in the administration of his duty. Bad notes will belie any plea he may make later as to the exercise of due care at the time, whereas good notes have time and again propped up the doctor who stood in peril, whose skill and care were in question.

It is the anæsthetist's duty to show proper care and a degree of skill commensurate with his station: it is incredibly careless of him not to let the world see that he has, in fact, exercised such care.

Now let us turn to another aspect of the anæsthetist's responsibility. It is plainly his duty to check his apparatus and his drugs, to see that his patient is as far removed as he can ensure from accident and unintentional overdosage. It is plainly also his duty to examine personally his patient in order that he may himself be in a position to assess any physical defect like heart disease or some respiratory disadvantage he may have to take into account. These are matters there is some general agreement upon, but there is another which is more often overlooked. The anæsthetist who is assisting the heroic or enthusiastic surgeon who may have a certain disregard for the responsibilities taken by his anæsthetist in such matters should call a halt as soon as any sign of danger to health arises—not danger to life. Prolongation of an operation for the purpose of teaching has caused death in one case I examined from a well-known London teaching hospital, and in another a period of some months' imbecility from cerebral anoxia preceded death owing to the anæsthetist being "muscle" out of reach of her subject by visitors who desired to get a closer view of the surgery. It is for the anæsthetist to put a stop to such dangers to his patient: over one and a half hours' teaching on a patient already gravely ill from strangulated femoral hernia constitutes a complete disregard for safety—and for an anæsthetist to find herself sitting on the floor out of reach of her patient because of enthusiasts craning over the patient to see some surgical procedure is almost Gilbertian. Neither

must be tolerated, and the anæsthetist who fails to warn the surgeon that his patient is slipping out of his grasp into danger fails also in his duty. It is negligent not to give such warning. Better to be alive with a half-completed or temporary surgical procedure than dead with a beautifully completed piece of surgical wizardry to carry to the grave.

I shall not enter the lists on the question of whether the anæsthetist's personal choice of the form of anæsthetic shall be final, or whether he is to bow to the wishes of a surgeon who has ideas of his own on the subject. In a well-balanced team such matters are discussed and settled to mutual satisfaction. But I have on many occasions where risky nose and throat surgery has been fatal, because blood or pus or some foreign body, such as packing, has obstructed the airway, heard differences of opinion on the ultimate responsibility for maintenance of an open or adequately intubated airway. I personally feel that it is a matter for the anæsthetist to see that his patient is given a fair chance of taking—and surviving—his anæsthetic, and that a free airway is one of the essentials upon which he must insist. Again, between two conscientious members of a team there will, no doubt, be mutual agreement over this, and a sharing of responsibility in the matter.

I have had, and continue to have, a steady experience of both anæsthetic irresponsibility and, unfortunately, of anæsthetic deaths of the preventable kind. I have already said that the latter are diminishing steadily with the advent of properly trained and duly qualified specialist anæsthetists, and it is good to think that my having the effrontery to say such things here concerns you as teachers rather than practitioners. No caution can be too strong or too oft repeated where real danger to an entirely helpless subject exists.

Dr. H. K. Ashworth welcomed the clear and concise presentation of facts, though he doubted whether figures shown by Dr. Keith Simpson as to the drugs used in 100 cases of deaths under anæsthesia gave a true percentage of causative agents. The figures for intravenous barbiturates were high in comparison with those of other agents, and a true picture could really only be obtained by knowing the total number of administrations of anæsthetics using all the various drugs mentioned in Dr. Simpson's figures. He also called attention to another point, namely the importance, particularly in a long hospital list, of the anæsthetist ascertaining the name of the patient before beginning the administration. He cited a recent case in which a hospital porter brought the wrong patient from two adjoining beds, and the mistake passed unnoticed until the patient had been anæsthetized.

Mr. J. Vincent Ramage (*Solicitor*) said: Mr. Heddy having pointed out that the high-water-mark of medical criminal negligence was reached in the case of *Rex v. Bateman* I venture to recall the facts of the case.

Mr. Bateman, a fully qualified registered medical practitioner, being called upon in the ordinary course of his profession to deliver a lady of a child, attended to the matter with such skill that not only did he invert and tear away the uterus but he brought away with it the greater portion of the descending colon. The patient having failed to survive the treatment the matter was enquired into by a Judge and Jury at the Old Bailey where Mr. Bateman was charged with manslaughter, and it was subsequently considered in the Court of Criminal Appeal with the result that it was solemnly decided that although Mr. Bateman had been negligent he had, nevertheless, used sufficient skill and judgment in the course of his relation to his patient as to make him not guilty of criminal negligence, and therefore not guilty of manslaughter and he was acquitted.

In view of the indulgence which on the basis of the decision in Bateman's case would appear to be extended by the legal profession to the medical profession upon matters of negligence, may I ask Mr. Heddy or Dr. Keith Simpson whether there has ever been a case in which an anæsthetist has been successfully proceeded against for either civil or criminal negligence? I would further ask, in view of the fact that the work of an anæsthetist is in the main only understood by him (thus protecting him to a considerable degree from informed criticism by those present at the time) whether there is the slightest chance of such proceedings ever being successfully brought against him in the future?

Mr. J. Simpson (*Chief Constable of Surrey*) spoke of what he considered to be a lack of discipline, or perhaps adequate machinery, within the medical profession. He had, as a Chief Officer of Police, had to deal with complaints against members of the profession including those alleging serious injury to health following the administration of anæsthetics. He instanced a case in which in a town within easy reach of a number of hospitals a doctor had removed a uterus, which he contended was affected by a malignant growth, in his surgery, administering the anæsthetic and carrying out the operation himself with the assistance only of his surgery "nurse", and returning his patient to her home within a few hours with no provision for home nursing. There were similar cases, including some of tonsillectomy running into the hundreds, from some of which serious ether burning and other complications were alleged to have occurred. These cases seemed to fall outside the ambit of the Criminal Law, and brother doctors who had to repair the damage, whilst being indignant, could apparently do nothing about it. He had referred cases which he had had prepared to the General Medical Council, but wondered whether he had either a right or a duty to do so.

Dr. Harold Sington drew attention to the fact that both Mr. Heddy and Dr. Keith Simpson had mentioned that the vast majority of the fatal cases had occurred when the anæsthetic had been administered by a doctor who was not a "recognized" specialist anæsthetist. From this the question arose as to why someone inexperienced in the practice of anæsthesia had been so employed.

He emphasized that the lay public did not sufficiently realize the importance of being anesthetized by an anæsthetist of the same professional attainments, experience and individual qualification as the surgeon enjoyed in his experience of surgery. And from this it must be concluded that the public should be instructed on these lines and suitable propaganda organized in order that patients should *demand* a specialist anæsthetist in the same way that they would only consent to be operated upon by a surgeon of proved skill.

Until this end had been achieved deaths under anæsthesia would continue to occur.

Dr. Donald Teare drew attention to the dangers which result when the newly qualified house physician is told by the surgeon the type and dose of anæsthetic to be given in any particular operation, and is not allowed to use what little experience he may have in such choice, this being particularly true of intravenous anæsthetics.

Mr. J. Milner Helme (*His Majesty's Coroner for (1) The City of London; (2) The County Borough of West Ham*) directed his remarks to the suggestion made by a previous speaker that sometimes the surgeon imposed his view upon the anæsthetist as to what anæsthetic should be used for an operation which the former was about to

perform, and he thought that this view also suggested that in such a case the surgeon would be responsible if the anæsthetist agreed to adopt his suggestion rather than use some other anæsthetic which he himself would have preferred.

Mr. Helme offered his opinion that in all cases the anæsthetist would be responsible for the anæsthetic actually used, and that, if he and the surgeon disagreed as to the anæsthetic to be used and the latter insisted on his choice there were two courses open to the anæsthetist:

(1) To agree to use the anæsthetic upon which the surgeon insisted, in which case, he (the anæsthetist) would make himself responsible for its effects.

(2) To refuse to administer the anæsthetic upon which the surgeon insisted, thus avoiding all responsibility and leaving those in charge of the case to find another anæsthetist.

Mr. Heddy, replying to points raised by the various speakers, emphasized the extremely high degree of negligence that was necessary for the establishment of criminal negligence and said he found it difficult to imagine circumstances in which an anæsthetist might lay himself open to a charge of manslaughter. He had been very interested in one question as to the propriety of a physician or a surgeon attempting to interfere with the anæsthetist's choice of agents or methods. His own feeling was that such interference was highly undesirable nowadays when the art and science of anæsthesia had reached a stage at which only a practising specialist was competent to form a judgment.

Dr. Keith Simpson, in reply, said he felt that Table II could leave little doubt that the anæsthetist undertook grave responsibilities and, on the whole, discharged them with no small credit. He had emphasized the vital need for conscience, as well as skill, and felt no warning on casual anæsthesia could ever be too strongly worded. His figures for fatalities were not to be taken to reflect the proportional risks of the various forms of anæsthesia, but to set out in plain terms certain common hazards some of which, he felt, were not adequately recognized.

## Section of Comparative Medicine

President—Professor WILSON SMITH, M.D., F.R.S.

[April 13, 1949]

### DISCUSSION ON LEPTOSPIROSIS

Dr. J. M. Alston:

#### General Survey

In November 1914, at the Imperial University in Kyushu, Japan, R. Inada and his colleagues demonstrated that a spirochæte—which they named the *Spirochæta icterohæmorrhagiae*—is the cause of Weil's disease. They cultured the organism and produced with it in guinea-pigs a disease closely resembling the human illness. They also demonstrated antibodies to it in the blood of patients and of animals experimentally infected.

In 1917 and 1918 Noguchi compared the *Spirochæta icterohæmorrhagiae* of Inada with similar organisms from British cases of Weil's disease in Flanders and with strains which he isolated from wild rats in the U.S.A. He found that from these three sources the organisms were the same in form and by immunological tests, and that they resembled no other organism already described except *Spirochæta biflexa*, which Wolbach and Binger (1914) had isolated in July 1913 from a fresh-water pond in Massachusetts. Noguchi gave to all these strains the generic name of *Leptospira*. The original strain of *L. biflexa* found by Wolbach and Binger did not survive its first subculture and the name is now used for some non-pathogenic *Leptospiras* which have been found in fresh water.

Since 1917 the genus *Leptospira* has been expanded by the addition of many more species. The differential criteria for these have been chiefly serological and much less pathogenicity in experimental animals and the protection of them by active and passive immunization; morphology and cultural characters have shown very few distinctions. Broadly speaking, this serological separation of species has been done most thoroughly in Japan, Malaya, the Netherlands East Indies, Holland and Denmark. The work has been based on agglutination, or agglutination and lysis, of strains by serum of immunized rabbits with or without absorption of antibodies. The results, therefore, lack the precision obtained in the *Salmonellas* by the chemical and physical separation of antigens.

To give an outline of the progress of the work I have made a table from several sources of the species in their approximate serological relationships. Such information was first published extensively by Walch-Sorgdrager in 1939 and has been continued by Borg-Petersen among others.

TABLE I.—FIRST IDENTIFICATION OF LEPTOSPIRAL SPECIES

| Species          | Date | Country    | Species        | Date | Country     |
|------------------|------|------------|----------------|------|-------------|
| Icterohæm.       | 1914 | Japan      | Akiyami A      | 1925 | Japan       |
| Salinem          | 1925 | N.E.I.     | =Autumnalis    |      |             |
| Canicola         | 1931 | Holland    | =Rachmat       | 1923 | N.E.I.      |
| Australis B      | 1934 | Queensland | Andaman B      | 1928 | Andaman Is. |
| =Zanoni          |      |            | =Grippotyphosa | 1928 | Russia      |
| Poi              | 1941 | Italy      | Australis A    | 1934 | Queensland  |
| Ballum           | 1943 | Denmark    | =Ballico       | 1934 | Queensland  |
| Hebdomadis       | 1918 | Japan      | Andaman A      | 1928 | Andaman Is. |
| =Akiyami B.      |      | Japan      |                |      |             |
| H.C.             |      | N.E.I.     | Pomona         | 1937 | Queensland  |
| Sajroe           | 1937 | Denmark    | =Mezzano       | 1940 | Italy       |
| Saxkoebing       | 1942 | Denmark    |                |      |             |
| Bataviae         | 1926 | N.E.I.     | Suis           | 1944 | Argentina   |
| =Swart v. Tienen |      | N.E.I.     | Bovis          | 1947 | Palestine   |
| =Mitis           | 1938 | Italy      |                |      |             |
| =Oryzeti         | 1939 | Italy      |                |      |             |

To this grouping it may be added that Borg-Petersen found *L. icterohæmorrhagiae* to exist in two forms which, because of their serological relationships, he named AB and A. Likewise *L. rachmat* is a partial form of *L. akiyami A*.

I shall now confine this brief outline of leptospirosis throughout the world mainly to the sources and methods of human infection and the forms which human infection takes.

perform, and he thought that this view also suggested that in such a case the surgeon would be responsible if the anæsthetist agreed to adopt his suggestion rather than use some other anæsthetic which he himself would have preferred.

Mr. Helme offered his opinion that in all cases the anæsthetist would be responsible for the anæsthetic actually used, and that, if he and the surgeon disagreed as to the anæsthetic to be used and the latter insisted on his choice there were two courses open to the anæsthetist:

(1) To agree to use the anæsthetic upon which the surgeon insisted, in which case, he (the anæsthetist) would make himself responsible for its effects.

(2) To refuse to administer the anæsthetic upon which the surgeon insisted, thus avoiding all responsibility and leaving those in charge of the case to find another anæsthetist.

Mr. Heddy, replying to points raised by the various speakers, emphasized the extremely high degree of negligence that was necessary for the establishment of criminal negligence and said he found it difficult to imagine circumstances in which an anæsthetist might lay himself open to a charge of manslaughter. He had been very interested in one question as to the propriety of a physician or a surgeon attempting to interfere with the anæsthetist's choice of agents or methods. His own feeling was that such interference was highly undesirable nowadays when the art and science of anæsthesia had reached a stage at which only a practising specialist was competent to form a judgment.

Dr. Keith Simpson, in reply, said he felt that Table II could leave little doubt that the anæsthetist undertook grave responsibilities and, on the whole, discharged them with no small credit. He had emphasized the vital need for conscience, as well as skill, and felt no warning on casual anæsthesia could ever be too strongly worded. His figures for fatalities were not to be taken to reflect the proportional risks of the various forms of anæsthesia, but to set out in plain terms certain common hazards some of which, he felt, were not adequately recognized.

## Section of Comparative Medicine

President—Professor WILSON SMITH, M.D., F.R.S.

[April 13, 1949]

### DISCUSSION ON LEPTOSPIROSIS

Dr. J. M. Alston:

#### General Survey

In November 1914, at the Imperial University in Kyushu, Japan, R. Inada and his colleagues demonstrated that a spirochæte—which they named the *Spirochæta icterohæmorrhagiæ*—is the cause of Weil's disease. They cultured the organism and produced with it in guinea-pigs a disease closely resembling the human illness. They also demonstrated antibodies to it in the blood of patients and of animals experimentally infected.

In 1917 and 1918 Noguchi compared the *Spirochæta icterohæmorrhagiæ* of Inada with similar organisms from British cases of Weil's disease in Flanders and with strains which he isolated from wild rats in the U.S.A. He found that from these three sources the organisms were the same in form and by immunological tests, and that they resembled no other organism already described except *Spirochæta biflexa*, which Wolbach and Binger (1914) had isolated in July 1913 from a fresh-water pond in Massachusetts. Noguchi gave to all these strains the generic name of *Leptospira*. The original strain of *L. biflexa* found by Wolbach and Binger did not survive its first subculture and the name is now used for some non-pathogenic *Leptospiras* which have been found in fresh water.

Since 1917 the genus *Leptospira* has been expanded by the addition of many more species. The differential criteria for these have been chiefly serological and much less pathogenicity in experimental animals and the protection of them by active and passive immunization; morphology and cultural characters have shown very few distinctions. Broadly speaking, this serological separation of species has been done most thoroughly in Japan, Malaya, the Netherlands East Indies, Holland and Denmark. The work has been based on agglutination, or agglutination and lysis, of strains by serum of immunized rabbits with or without absorption of antibodies. The results, therefore, lack the precision obtained in the *Salmonellas* by the chemical and physical separation of antigens.

To give an outline of the progress of the work I have made a table from several sources of the species in their approximate serological relationships. Such information was first published extensively by Walch-Sorgdrager in 1939 and has been continued by Borg-Petersen among others.

TABLE I.—FIRST IDENTIFICATION OF LEPTOSPIRAL SPECIES

| Species          | Date | Country    | Species        | Date | Country     |
|------------------|------|------------|----------------|------|-------------|
| Icterohæm.       | 1914 | Japan      | Akiyami A      | 1925 | Japan       |
| Salinæm          | 1925 | N.E.I.     | =Autumnalis    |      |             |
| Canicola         | 1931 | Holland    | =Rachmat       | 1923 | N.E.I.      |
| Australis B      | 1934 | Queensland | Andaman B      | 1928 | Andaman Is. |
| =Zanoni          |      |            | =Grippotyphosa | 1928 | Russia      |
| Poi              | 1941 | Italy      | Australis A    | 1934 | Queensland  |
| Ballum           | 1943 | Denmark    | =Ballico       | 1934 | Queensland  |
| Hebdomadis       | 1918 | Japan      | Andaman A      | 1928 | Andaman Is. |
| =Akiyami B.      |      | Japan      |                |      |             |
| H.C.             |      | N.E.I.     | Pomona         | 1937 | Queensland  |
| Sejroe           | 1937 | Denmark    | =Mezzano       | 1940 | Italy       |
| Saxkoebing       | 1942 | Denmark    |                |      |             |
| Bataviæ          | 1926 | N.E.I.     | Suis           | 1944 | Argentina   |
| =Swart v. Tienen |      | N.E.I.     | Bovis          | 1947 | Palestine   |
| =Mitis           | 1938 | Italy      |                |      |             |
| =Oryzeti         | 1939 | Italy      |                |      |             |

To this grouping it may be added that Borg-Petersen found *L. icterohæmorrhagiæ* to exist in two forms which, because of their serological relationships, he named AB and A. Likewise *L. rachmat* is a partial form of *L. akiyami A*.

I shall now confine this brief outline of leptospirosis throughout the world mainly to the sources and methods of human infection and the forms which human infection takes.

The spread of *L. icterohæmorrhagiæ* to man is almost entirely due to the fact that some small rodents and a few other animals harbour the organism for a longer or shorter time and excrete it in the urine. By far the most important are rats, of which many species harbour the organism in most countries of the world, with the chief exception of most parts of Africa. Much less often field-mice and ferrets have been found infected. Next to rodents, dogs and wild and silver foxes suffer infection. Pigs, horses, cattle and perhaps cats are rarely infected.

Of some of the other *Leptospiras*, also, an important source of infection is the rat, including *L. salinem*, *L. akiyami A*, *L. bataviæ* in the Netherlands East Indies, and *L. australis A* and *B* in Queensland. Otherwise, *Leptospiras* have as their principal known carriers, various mice for *L. hebdomadis*, *L. sejroe*, *L. saxkoebing*, *L. ballum* and for *L. bataviæ* in Europe, dogs for *L. canicola*, pigs for *L. suis* and for *L. pomona* in Europe, cattle for *L. bovis*. *L. bataviæ* has also been found in dogs and cats in the Netherlands East Indies.

There are several species for which an animal host has not yet been found in some of the localities where they are frequent. Such are *L. poi* and the two species from the Andaman Islands. These *Leptospiras* are particularly associated with human infections after long-lasting contact with water in rice fields and swampy land. The absence of a known animal host has led some writers such as Van Riel (1948) to claim that, in general, the survival of pathogenic *Leptospiras* in water is more important to man than their presence in animals which may contaminate the water. This is probably too extreme, but it emphasizes that in almost all circumstances infection from animal carrier to man is not through direct contact but is by *Leptospiras* which have been excreted by animals on to damp ground or into water which allows the organism to survive.

The rodents which are the commonest carriers suffer very little from their leptospiral infection and may excrete the organisms for a large part of their lifetime. To some of the other animals—dogs, pigs and cattle—*Leptospiras* are more pathogenic.

The route of infection of human beings can be generally exemplified by *L. icterohæmorrhagiæ*. The skin, especially through cuts, abrasions, bites or sodden surfaces, is the usual site of entry. Accidental infections of workers in laboratories have shown that the conjunctivæ and the mouth may give entrance, and infection in bathing may sometimes be by these routes. Entry by the lungs is suspected. Infection by contact between human beings is almost unknown.

One purpose of this outline is to emphasize that in Great Britain only two species—*L. icterohæmorrhagiæ* and *L. canicola*—have yet been identified in contrast with at least ten on the Continent of Europe. I have, therefore, made a list of British Muridæ and against the appropriate names placed the species of *Leptospiras* found in various continental countries. Table II shows that four species of *Leptospiras* unknown in nature in this country occur abroad in muridæ which are to be found in various parts of the British Isles and that two more *Leptospiras* have been found on the Continent in rodents nearly related to British species.

TABLE II

| British Muridæ                      | <i>Leptospiras</i> in<br>Continental Europe                        |
|-------------------------------------|--------------------------------------------------------------------|
| MICROTINÆ (voles and lemmings)      |                                                                    |
| <i>Eutamias glareolus</i>           | <i>L. grippotyphosa</i>                                            |
| <i>Microtus hirtus</i>              |                                                                    |
| <i>Microtus agrestis</i>            |                                                                    |
| <i>Arvicola amphibius amphibius</i> |                                                                    |
| <i>Arvicola amphibius retina</i>    |                                                                    |
| MURINÆ (rats and mice)              |                                                                    |
| <i>Apodemus sylvaticus</i>          | { <i>L. grippotyphosa</i><br><i>L. sejroe</i><br><i>L. bataviæ</i> |
| <i>Apodemus flavicollis wintoni</i> |                                                                    |
| <i>Micromys minutus</i>             | <i>L. bataviæ</i>                                                  |
| <i>Rattus rattus</i>                |                                                                    |
| <i>Rattus norvegicus</i>            |                                                                    |
| <i>Mus musculus</i>                 |                                                                    |

ALSO, Muridæ, nearly related to those above, are on the Continent infected with *Leptospiras*, thus:

|                                |                                            |
|--------------------------------|--------------------------------------------|
| <i>Apodemus flavicollis</i>    | <i>L. saxkoebing</i>                       |
|                                | <i>L. ballum</i>                           |
| <i>Mus musculus spicilegus</i> | { <i>L. saxkoebing</i><br><i>L. sejroe</i> |



The most virulent species towards man is *L. icterohæmorrhagiæ* and next to it are akiyami A, rachmat, salinem and, in the East, bataviæ. Their greater virulence compared with the remainder is shown by higher case mortality, and by more jaundice and more acute nephritis. At the same time, milder infections without jaundice and with very little nephritis constitute at least half the cases of such infections, with mild meningitis as the chief feature of some of them. In contrast to the species named, the others, including infections in Europe by *L. bataviæ*, cause little or no jaundice, slight nephritis and very few deaths. The chief features in these diseases are fever, malaise and muscular pains, or mild meningitis. It is the cases with meningitis which are most likely to be found when infections by a particular species of mildly virulent *Leptospiras* are first recognized; this is the case in Great Britain at present with *L. canicola*.

The history of human leptospirosis in Great Britain consists of the knowledge of infections of *L. icterohæmorrhagiæ* since 1922 and of infections by *L. canicola* since 1945.

In 1922 a man was infected with *L. icterohæmorrhagiæ* by immersion in the Thames and the organism was found in his blood by H. C. Brown. In 1924 equally well proved infections of coal-miners and others in E. Lothian were reported by Gulland and Buchanan. After a gap of ten years, Fairley (1934) reported that a sewerman in London died of the disease, as established by the isolation of the infecting *Leptospira* and by serological tests; also, serological tests indicated previous infection in 8 other sewermen. In 1935, H. C. Brown reported on the value of the adhesion test and Schüffner's agglutination test for serological diagnosis. As a result he was able in seven months to diagnose the infection in 40 patients living in all parts of England and Wales. Since then diagnosis has been practised chiefly in about six laboratories. From the published and unpublished records I have collected nearly 1,000 proved cases of leptospirosis icterohæmorrhagica from July 1933 to July 1948. Three-quarters of these have been analysed as to the patient's occupation at the time of infection and a relation to rat infestation in wet areas is evident in most (Table III).

TABLE III.—OCCUPATION RELATED TO 716 CASES OF WEIL'S DISEASE IN THE BRITISH ISLES  
JULY 1933—JULY 1948

| Occupation or cause                         | Per cent of total |
|---------------------------------------------|-------------------|
| Fish-worker .. .. .                         | 30                |
| Butcher, tripe-scraper, &c. .. .            | 3                 |
| Coal-miner .. .. .                          | 20                |
| Sewer worker .. .. .                        | 11                |
| Army .. .. .                                | 9                 |
| Royal Navy .. .. .                          | 2                 |
| Royal Air Force .. .. .                     | 2                 |
| Bathing, paddling, &c., in fresh water .. . | 6                 |
| Farm-worker .. .. .                         | 6                 |
| Worker in water including canal, &c. .. .   | 2                 |
| Bite, &c., of rat, dog or ferret .. .. .    | 2                 |
| Builder, &c. .. .. .                        | 1                 |
| Gardener, &c. .. .. .                       | 1                 |
| Laboratory worker .. .. .                   | 1                 |
| Miscellaneous, e.g. bottle-washer .. .. .   | 4                 |
|                                             | <hr/> 100         |

The infection has been found widely in the British Isles. In Aberdeen, Davidson and Smith (1939) have detected over 200 instances among men and women handling white fish in unhygienic sheds. Infections in coal-miners in wet and rat-infested pits have been found chiefly in the West of Scotland by R. D. Stuart and in Northumberland and Durham and in South Wales by H. C. Brown and J. C. Broom. In London, sewer workers provide most of the patients and my own experience has been largely with them. In the Services, camps, bivouacs, rat-infested ships and aerodromes have caused infections. Bathing and paddling in fresh water cause infections in the summer. In the other occupations, also, contact is possible with *Leptospiras* excreted by rats.

Males are much oftener infected than females, due to the greater exposure of men to infection in some occupations. For instance, Broom and I found that of 189 cases during the years 1940-46 only 4.4% were women.

Patients of all ages from 4 years to 78 years have been recorded in this country.

There is a seasonal variation of incidence. Bathing in fresh water in the summer and autumn obviously contributes to this, but I found in sewer workers during 1934-45 a clear preponderance in the months of the second half of the year. Similar variation has been found in the fish-workers in Aberdeen and in cases generally in Holland and Denmark.

The accuracy of the fatality rates depends on the number of mild infections which are included. Death does not occur without jaundice even when meningitis is present. In two

series of 256 cases in this country between 1933 and 1946 the death-rate was 18%; over 90% of all the patients were jaundiced. Age increases the case mortality rate. Broom and I found a rate of 16% below the age of 46 and 42% later.

Buzzard and Wylie reported 5 instances of meningitis, without jaundice, that occurred in this country in 1946. This form was previously known elsewhere. Broom and I have investigated four other instances. A big proportion of such clinical forms are due to bathing in fresh water. Confusion with acute anterior poliomyelitis has occurred before serological diagnosis was made.

The history in Great Britain of undoubted human infections by *L. canicola* is much shorter. This species of *Leptospira* was first isolated in 1931 by Klarenbeek and Schöffner from the urine of a dog, and in 1934 the same Dutch workers and two colleagues recorded the first infections known in human beings. Since then 150 cases have come to light. These have been about 50 each in Holland and Denmark and the remainder in other European countries, the U.S.A., Argentine and China. It is presumed that dogs are the source of all human infections. Entry of the *Leptospira* is by the skin or sometimes by the eye or mouth. Most cases occur in the second half of the year. Infection is usually domestic and equal in the sexes. Mild meningitis is the most prominent feature in two-thirds of the cases found; conjunctivitis, iritis and skin rashes are frequent. Only one death has been recorded.

As regards Great Britain, in 1945 a boy fell ill of this infection twelve days after swimming in the Thames, as recorded by Baber and Stuart (1946) and in 1947 and early 1948 4 more such cases occurred in England. I had some part in examining 3 of these with J. C. Broom and they were all 4 published in 1948. Since then I have found 3 more cases and Broom several others. In 5 out of 7 patients there was contact with a dog, which was shown to be infected by *L. canicola* in 2 instances and had been ill in 2 more. So far as I know, meningitis has been the most obvious evidence of disease, and recovery has occurred in the published cases and in others which I observed.

#### REFERENCES

- BABER, M. D., and STUART, R. D. (1946) *Lancet* (ii), 594.  
 BORG-PETERSEN, C. (1944a) *Ugeskr. Læg.*, 106, 617.  
 — (1944b) *Acta path. microbiol. scand.*, 21, 165, 504.  
 —, and CHRISTENSEN, H. I. (1939) *Ugeskr. Læg.*, 101, 697.  
 BROOM, J. C., and ALSTON, J. M. (1948) *Lancet* (ii), 96.  
 BROWN, H. C. (1935) *Brit. med. J.* (i), 411.  
 BUZZARD, E. M., and WYLIE, J. A. H. (1947) *Lancet* (ii), 417.  
 DAVIDSON, L. S. P., and SMITH, J. (1939) *Brit. med. J.* (ii), 753.  
 DHONT, C. M., et al. (1934) *Ned. Tijdschr. Geneesk.*, 78, 5197.  
 FAIRLEY, N. H. (1934) *Brit. med. J.* (ii), 10.  
 GULLAND, G. L., and BUCHANAN, G. (1924) *Brit. med. J.* (i), 313.  
 INADA, R., et al. (1916) *J. exp. Med.*, 23, 377.  
 KLARENBECK, A., and SCHÖFFNER, W. (1933) *Ned. Tijdschr. Geneesk.*, 77, 4271.  
 LAURENT, L. J. M., et al. (1948) *Lancet* (ii), 48.  
 NOGUCHI, H. (1917) *J. exp. Med.*, 25, 755.  
 — (1918) *J. exp. Med.*, 27, 609.  
 VAN RIEL, J. (1948) *Brux. méd.*, 28, 2054.  
 WALCH-SORGDRAGER, B. (1939) *Bull. Hlth. Org. League of Nations*, 8, 143.  
 WOLBACH, S. B., and BINGER, C. A. L. (1914) *J. med. Res.*, 30, 23.

Miss J. O. Joshua:

#### Introduction

Leptospiral infection in dogs in this country has received very little attention, either in the literature or from clinicians.

In 1925 Okell, Dalling and Pugh described *L. icterohæmorrhagie* infection in dogs, to which they gave the name of "Yellows". They described the condition as being sporadic in adults and enzootic in young dogs. In the acute form they found initial high temperature, severe depression, muscular pain, vomiting and thirst. Death often occurred before icterus developed. The subacute form was similar but icterus developed in two to six days.

Typical post-mortem findings were a hæmorrhagic inflammation of the alimentary tract, jaundice and albuminuria; lung hæmorrhages were a regular finding; intussusception was common in puppies. This has remained the classical picture of leptospiral jaundice in dogs until this day, and apart from occasional clinical reports of isolated cases from time to time canine leptospirosis remained a neglected subject until Stuart in 1946 stimulated interest by his report of the examination of serum from street dogs in Glasgow, 52% of which showed agglutinins to one or other type of *Leptospira*.

In 1947 Freak and I described a series of cases of *L. canicola* infection, with special reference to their treatment by penicillin, and later, in 1948, drew attention to the existence of a form of infection with *L. icterohæmorrhagie* which gave a purely renal syndrome and was clinically

indistinguishable from canicola fever. In 1948 Mills described the clinical aspects of both *L. icterohæmorrhagiæ* and *L. canicola* infection in dogs.

I must at this stage acknowledge the debt which I, personally, owe to Dr. Margrit Scheitlin, of Zurich, whose visit to my practice in 1946 resulted in my recognition of leptospirosis as a by no means uncommon disease of dogs in this country. Since then clinicians in many parts of the country have recognized leptospirosis due to both types of organism, as being of relatively high incidence in the canine population.

I should like to deal briefly with the incidence of leptospiral infection as judged on the results of the agglutination test carried out on 100 random blood samples; my own views as to the method and spread of infection; a brief indication of the clinical features of the disease in dogs, and finally, a few words on the public health angle.

#### Incidence

The following figures are based on 100 blood samples taken from dogs of all types and ages, some healthy, but most destroyed for a wide range of conditions; the 100 samples include bloods from cases of active leptospiral infection. In view of the accepted specificity of the agglutination test I have taken the somewhat arbitrary line of assuming that the presence of agglutinins, no matter in how low a titre, is an indication that the dog has at some time in its life come into contact with the organism, but not necessarily that clinical disease has occurred. In this way it is possible to get some idea of the prevalence of the organism.

43 dogs showed agglutinins to one or other species of *Leptospira*. Of these 31 showed a higher titre to *L. canicola*, 8 to *L. icterohæmorrhagiæ* and 4 showed agglutinins, in low titre only, equally to both organisms.

The sex incidence does not at present appear to show any very significant difference, although the percentage of reactors in males is slightly higher. Of the 100 bloods 61 were from dogs and 39 from bitches; of the 43 positives 29 were dogs and 14 bitches; i.e. approx. 48% dogs and 36% bitches were positive.

The age incidence is probably of some significance quite apart from the fact that older animals have had a longer period of potential exposure to infection. Only three dogs under 1 year old showed agglutinins, all were males and all showed clinical evidence of the disease. None was under 6 months.

There were 13 positives under 5 years of age, 11 dogs and 2 bitches. In view of later comments on possible methods of infection it is of some interest to note that these two positive bitches were a Pekingese and a Scottish Terrier, both low-to-ground breeds. Of these 13 in this age-group only two were dogs not suspected of clinical leptospirosis.

Of the 30 positives of over 5 years of age only 5 were considered to be showing symptoms attributable to recent leptospiral infection. Very many of the remaining 25 had never shown evidence of an illness which could have been attributed to leptospirosis. Naturally, a full clinical history was not obtained in all these cases. These figures do suggest, however, that a subclinical infection can occur in dogs, a matter of considerable importance in considering the spread of infection.

The over-all figure of 43% reactors agrees very closely with Stuart's findings in Glasgow, the slightly lower total figure in my case probably being due to the inclusion of a larger number of dogs 1 year old or less, 21 in my series as compared with 8 in that of Stuart. The ratio of canicola to icterohæmorrhagiæ infection is also strikingly similar. Similar figures from other parts of the country would be of great interest.

#### Methods of Infection and Spread

*L. icterohæmorrhagiæ*.—It has always been considered that infection by this organism in dogs is acquired from rats, the natural reservoir of this species, usually from food or ground contaminated by rat urine. This is probably true in the case of acute outbreaks of leptospiral jaundice, when direct or indirect contact with rats can usually be traced. In my series of cases, however, of the subacute renal type which have subsequently proved to be due to *L. icterohæmorrhagiæ* infection, there have been several instances where it has been quite impossible to trace any connexion with rats at all, no matter how remote, and I have felt that in some, at least, of these, indirect dog to dog transmission via wet ground, &c. has been responsible.

*L. canicola*.—The dog is the only known natural host of this species, yet it is said that the carrier state persists only for a relatively brief period, viz. about three months; Wirth records a leptospiuria persisting for six and a half months, in one case; Walch-Sorgdrager records persistence up to four months.

Judged by the peculiar area incidence of canicola fever in dogs which has been observed by a number of clinicians these facts do not appear to me to represent the whole story. From

clinical observation in my own and other practice areas I cannot help feeling that *L. canicola* is capable of survival outside the animal body for very long periods, in suitable environment, viz. damp ground and stagnant water.

The incidence of the disease in dogs coming from areas where they have access to ponds, &c., is too marked to be mere coincidence. My findings agree with those of Winsser, that it is possible in a very high proportion of clinical cases to trace a history of immersion, partial or complete, in stagnant or static water some four to six weeks before the onset of clinical symptoms. Curiously enough, drinking such water does not appear to cause infection, since it is common to know of dogs which habitually drink from ponds from which other animals appear to have contracted infection following immersion, yet remain healthy.

This suggests that the route of infection is more frequently via the mucosa of the genito-urinary tract than via the alimentary canal, a suggestion which is borne out by the figures for age incidence and certain rather general observations on breed incidence.

After sexual maturity in the dog (at about 8-10 months) the act of urination may well be the cause of actual contact between the preputial hairs and the wall or lamp posts against which other dogs have previously urinated, in my view a very probable source of infection. This theory is borne out by the incidence of a number of cases of leptospirosis occurring within a short period in dogs living within a few hundred yards of one another, and yet between which there has been no actual contact, nor is there any source of water-borne infection as suggested previously. Wirth suggests that the habit of dogs to sniff at urine or the external genitalia of other dogs may be responsible for the acquisition of infection.

Further support for this suggested route of infection lies in breed incidence. It has already been noted that the only cases of leptospirosis occurring in young bitches were in low-to-ground breeds; in addition veterinary clinicians have for many years recognized a very high breed incidence of acute and subacute nephritis in the Scottish Terrier; since recognizing leptospiral infection I have been able to incriminate the organism in all such cases in this breed. It therefore seems probable that low-to-ground breeds, particularly the Scottie, which carries a very heavy "whisker" around the external genitalia in both sexes, are very prone to infection via the genito-urinary tract.

My views on the persistence of infection in water or other suitable ground outside the animal body are borne out by instances such as the following: unfortunately I have no accurate data as to the period between the cases cited, but on one particular premises three dogs had been lost in succession, certainly with a lapse of some weeks between the cases, from the disease known to clinicians as Stuttgart disease (which I now believe to be the acute form of canicola fever); the last case only was tested and was positive for *L. canicola* infection; in the grounds in question there is a pond to which the dogs had access, and there seems little doubt that this was the source of infection, the organism having remained viable in it for a matter of weeks, at least.

In my practice area there has been some seasonal variation in the incidence of the disease, the great majority of cases occurring between late October and April (inclusive), i.e. the wetter periods of the year. I do not think that this finding is borne out by all clinicians, but from personal observation it does suggest greater viability of the organism in wetter periods of the year. It is noteworthy that during this unusually dry autumn and winter (1948-49) my cases of leptospirosis have been few. Many damp areas and small ponds in my locality are dried up.

#### *Clinical Features of Leptospirosis in Dogs*

Acute *L. icterohæmorrhagicæ* infection has already been adequately described by Okell, Dalling and Pugh. Acute canicola fever in my view is the syndrome known to clinicians in this country as Stuttgart disease, comprising acute vomiting, rapid dehydration and collapse, occasionally the passage of blood-stained faeces, with finally, if the dog survives long enough, rapid necrosis and sloughing of the buccal mucosa and tongue. The mortality rate, prior to the introduction of penicillin therapy, was high, death occurring in thirty-six hours to four days.

Subacute disease, caused by either organism, is more common and it does not appear to be possible to diagnose the causal organism on clinical grounds alone. The syndrome is predominantly a renal one, although widespread tissue damage in many organs does occasionally occur, and icterus may even be found in cases of canicola fever, due to liver damage. Meningeal symptoms have not been observed. Temperature rise may be noted early in the disease, but seems not to be invariable.

Symptoms commonly observed include profound depression, vomiting, muscular pain in the early stages, and a tucked-up appearance usually associated with pain in the renal area; thirst may be in abeyance or excessive, with corresponding oliguria or polyuria.

I have not noted the episcleral injection described by Winsser as being a regular feature

in cases of leptospirosis, although it does occasionally occur and is very characteristic. Discoloration of the tongue, either the tip or the entire dorsum, is a very common feature, the tongue becoming brick-red or brownish and dry in appearance. Ulceration of the buccal mucosa is common.

Marked enlargement of the kidneys may occur and it is often possible to palpate the left kidney very easily. Abdominal palpation in dogs not grossly fat often reveals marked aortic pulsation, but what is the diagnostic significance of this feature I am as yet undecided; I do not recall having noted it in other diseases. It seems probable that some cases of apparently simple vomiting and depression, diagnosed variously as gastritis, liver attacks, &c., may be instances of very mild leptospiral infection.

Urine analysis is of little value in diagnosis, specific gravity varying with the fluid intake; albuminuria may be present in slight degree or may be absent; traces of bile pigment are common.

In the majority of such cases death, when it occurs, is due to uræmia. The ætiological significance of a leptospiral infection in cases of nephritis in old dogs is at yet uncertain. Of a total of 10 nephritis cases in my series of blood examinations (not including current leptospiral infection) 5 were positive and 5 negative for antileptospiral agglutinins.

*Treatment.*—In canicola fever penicillin is almost a specific, and in my view is useful as a diagnostic aid for differentiation between the two organisms, since the response of *L. icterohæmorrhagie* infection is absent or slight; response in primary canicola cases is spectacular.

Serum in *L. icterohæmorrhagie* cases gives very variable results, possibly due to rather late administration in some cases. Otherwise treatment is carried out on symptomatic lines.

I do not propose to discuss diagnosis other than to say that up to the present I have relied upon the clinical picture, confirmed by blood examination at a suitable stage in the disease. I am not yet clear as to the effect penicillin therapy has in cutting short antibody formation and thus masking the result of subsequent serological examination. I feel that detection of the organism in blood or urine is a matter for an experienced bacteriologist, and is not a method likely to be of value to the average clinician.

#### Public Health Considerations

The veterinary clinician is faced with a somewhat awkward problem in advising clients as to the possibility of transmission of infection from dog to man.

That a very definite human hazard does exist is undeniable, yet looking back over several years of practice I can think of no case where I could feel certain an owner had contracted leptospiral infection from a dog. Possibly the tardy recognition of canicola fever in man in this country may have masked the true position. In these circumstances I do not feel one should adopt anything of an alarmist attitude, yet we should be remiss in our duty if we did not point out to the owner of an infected dog that human infection is possible.

The course I adopt is to warn owners fairly strongly in cases where I suspect *L. icterohæmorrhagie* as the causal organism, in view of the relative seriousness of Weil's disease in man. In the case of canicola infection I point out that while human infection is a possibility it is not a probability.

In view of the fact that infection is likely to be acquired from urine I advise accordingly, and recommend the wearing of rubber gloves in cases where the dog is very ill and nursing entails frequent contact with urine, soiled bedding, &c. I cannot feel that we should panic owners into having leptospirosis cases destroyed needlessly, yet we must recognize that we have a definite public health duty in connexion with this disease. I should like to hear the views of medical members on this point.

May I conclude by expressing my thanks to Dr. Broom for carrying out the serological examinations I have quoted and for his help and advice during the few years I have been interested in this disease.

#### REFERENCES

- FREAK, M. J., and JOSHUA, J. O. (1948) *Vet. Rec.*, 60, 252.  
 JOSHUA, J. O., and FREAK, M. J. (1947) *Vet. Rec.*, 59, 595.  
 MILLS, S. (1948) *Vet. Rec.*, 60, 267.  
 OKELL, C. C., DALLING, T., and PUGH, L. P. (1925) *Vet. J.*, 81, 3.  
 STUART, R. D. (1946) *Vet. Rec.*, 58, 132.  
 WALCH-SORGRAGER, B. (1939) *Bull. Hlth. Org. League of Nations*, 8, 143.  
 WINSSER, J. (1943) *Z. InfektKr. Haustiere*, 60, 103.  
 WIRTH, D. (1939) *Wien. tierärztl. Mschr.*, 24, 97.

Dr. C. Borg-Petersen (State Serum Institute, Copenhagen):

*Experience of Leptospirosis in Denmark*

Danish experience of leptospirosis practically speaking dates from 1934. Before that time only a few cases of Weil's disease had been diagnosed in our country, and consequently it was the general belief that the occurrence of this disease was extremely rare. In the summer of 1934, the German microbiologist, Zuelzer, visiting the Danish State Serum Institute, proved that Danish rats were infected with *Leptospira icterohæmorrhagie* to about the same extent as rats in other countries. The attention of medical men in Denmark was immediately drawn to this fact, and they were called upon to send in to the Institute samples of blood from suspect cases. These samples were examined by Professor Schüffner at the Institute of Tropical Hygiene at Amsterdam, and during the last half of 1934 no less than 14 cases of Weil's disease were diagnosed. Thus it was obvious that the disease was in no way uncommon in Denmark, and in 1935 a diagnostic *Leptospira* laboratory was established at the State Serum Institute.

In 1936 it was found that leptospirosis was prevalent among dogs in Denmark, so from 1937 the Danish State Veterinary Serum Laboratory took over the bacteriological *Leptospira* diagnosis in dogs and other animals.

Since 1934, leptospirosis has been bacteriologically verified in a total number of 808 human patients, and this figure probably represents the majority of diagnosed cases in Denmark, but of course actually far more cases of the disease have occurred. The yearly number of diagnosed cases is shown in the first column of Table I.

I have to state that, naturally, we have not isolated *Leptospiras* from all the 808 patients, only from 81 among them; in the majority of cases the diagnosis is founded on the demonstration of antibodies in sera from the patients. For the seroreaction we used the agglutination-test with living cultures and with microscopical reading with dark-field illumination.

In the beginning these seroreactions were made with *L. icterohæmorrhagie* and *L. canicola* only. In 1935 and 1936 only infections by *L. icterohæmorrhagie* were found, and practically all of these were jaundiced cases. Now, as it was known from other countries that the majority of cases of leptospirosis *icterohæmorrhagica* did not show any jaundice, it was obvious that only severe infections had been diagnosed in Denmark. Consequently, in order to detect the cases without jaundice as well, we examined in 1937 about 8,000 sera sent to the Institute for the Widal reaction. In this way we succeeded in finding, first: 10 infections by *L. icterohæmorrhagie*, 8 of which were without jaundice, and secondly: 6 of *L. canicola*, all without jaundice. The examination of Widal sera was continued in the following years and revealed many cases which would not otherwise have been diagnosed.

In the course of the period 1936-37, we had met with several cases which clinically were typical of leptospirosis, but which showed equal, rather weak, seroreactions to both *L. icterohæmorrhagie* and *L. canicola* and which could not therefore be classified. This fact was explained towards the end of 1937, when, from the blood of a patient, we cultivated a *Leptospira* strain serologically different from *icterohæmorrhagie* and *canicola*. With this strain the sera just mentioned gave strong positive reactions. On comparison with the other serological types hitherto described, the new strain was found to differ from all of them and, therefore, had to be regarded as a new serological type, which we named *L. sejroe* after the locality in Denmark where it was first discovered.

Naturally, a strain of *L. sejroe* was at once included among the strains used in our routine serum test; and in the following years a considerable number of infections caused by this type were diagnosed, as will be seen in Table I. In 1939 *L. grippotyphosa*, in 1941 *L. bataviae* and *L. pomona*, and in 1945 *L. poi* were added, since infections caused by these types had been found in other parts of Europe. From Table I it will be seen that only a few infections by *L. grippotyphosa*, *L. bataviae*, and *L. poi* have been found in Denmark, while we have not seen any case of leptospirosis *pomona*. Nor have we seen any human infections caused by type ballum, which was found in 1943 in Denmark in a mouse, and which has since 1944 been included among the serum-test strains. The last column in Table I shows some cases which for various reasons could not be classified.

The classification in serological types was made under the impression of the pluralistic conception current in the latter part of the 'thirties, according to which the prognosis and the epidemiology of the leptospiroses are related to the serological type of the infecting *Leptospiras*, and we shall now see whether it is possible to find such relations in our material.

As for the clinical features, we have at the State Serum Institute only very incomplete data about the patients, but for all the cases examined we know: (1) Whether the patient survived or died from the infection, and (2) whether the patient was jaundiced or not. This information is presented in Table II.

TABLE I

|         | Total | Ictero-hæm. | Canicola | Sejroe (&c.) | Grippotyphosa | Bataviæ | Poi | Pomona | Ballum | Type? |
|---------|-------|-------------|----------|--------------|---------------|---------|-----|--------|--------|-------|
| 1934    | 14    | 14          |          |              |               |         |     |        |        |       |
| 1935    | 14    | 14          |          |              |               |         |     |        |        |       |
| 1936    | 24    | 22          |          | 2            |               |         |     |        |        |       |
| 1937    | 42    | 31          | 6        | 5            |               |         |     |        |        |       |
| 1938    | 30    | 16          | 2        | 10           |               |         |     |        |        | 2     |
| 1939    | 46    | 20          | 5        | 19           |               |         |     |        |        | 2     |
| 1940    | 37    | 21          | 4        | 9            | 1             | 1       |     |        |        | 1     |
| 1941    | 24    | 12          | 4        | 8            |               |         |     |        |        |       |
| 1942    | 48    | 11          | 2        | 34           | 1             |         |     |        |        |       |
| 1943    | 253   | 16          | 24       | 198          | 9             | 2       |     |        |        | 4     |
| 1944    | 102   | 24          | 11       | 59           | 1             | 5       |     |        |        | 2     |
| 1945    | 78    | 18          | 25       | 28           | 1             | 5       | 1   |        |        |       |
| 1946    | 43    | 16          | 11       | 10           | 1             | 3       | 1   |        |        | 1     |
| 1947    | 22    | 11          |          | 11           |               |         |     |        |        |       |
| 1948    | 31    | 8           | 1        | 21           | 1             |         |     |        |        |       |
| Total   | 808   | 254         | 95       | 414          | 15            | 16      | 2   | 0      | 0      | 12    |
| % Men   |       | 86          | 57       | 66           | 100           | 100     |     |        |        |       |
| % Women |       | 14          | 43       | 34           | 0             | 0       |     |        |        |       |

TABLE II

|                | 1934-38 |         |       | 1939-43 |         |       | 1944-48 |         |       |
|----------------|---------|---------|-------|---------|---------|-------|---------|---------|-------|
|                | Total   | Icterus | Fatal | Total   | Icterus | Fatal | Total   | Icterus | Fatal |
| Ictero-hæm. .. | 97      | 79      | 23    | 80      | 48      | 9     | 77      | 39      | 5     |
| % .. ..        |         | 81      | 24    |         | 60      | 11    |         | 51      | 6     |
| Canicola ..    | 8       | 1       | 0     | 39      | 5       | 0     | 48      | 6       | 0     |
| % .. ..        |         | 13      | 0     |         | 13      | 0     |         | 13      | 0     |
| Sejroe ..      | 17      | 2       | 0     | 268     | 35      | 2     | 129     | 19      | 1     |
| % .. ..        |         | 12      | 0     |         | 13      | 1     |         | 15      | 1     |
| Grippotyphosa  |         |         |       | 11      | 1       | 0     | 4       | 0       | 0     |
| Bataviæ ..     |         |         |       | 3       | 0       | 0     | 13      | 3       | 0     |
| Type ? ..      | 2       | 2       | 0     | 7       | 3       | 3     | 3       | 1       | 0     |

As regards leptospirosis icterohæmorrhagica, the figures for the fatality rate show a definite falling tendency for the three periods in question. Whether this corresponds to a real change in virulence or whether it is caused wholly or partially by other factors, I do not propose to discuss now. As regards the canicola type, we have not had any fatal cases yet, and for the sejroe type the fatality rate seems to be about 1%. The number of cases of the other types is too small to allow of any estimate of the fatality rate.

It will be seen that in the life and death prognosis there is a definite distinction between the icterohæmorrhagæ type on the one side and the canicola and sejroe types on the other side.

As for jaundice, this syndrome was seen in the three five-year periods in 81%, 60% and 51% of the icterohæmorrhagæ cases, whereas in the canicola and sejroe infections it was only observed in 12 to 15% of the cases. Here I must add that in most of the cases of canicola and sejroe infections the observed jaundice was very slight, in many instances the patients only showed jaundiced scleræ. In the icterohæmorrhagæ infections, jaundice was generally much more pronounced. Also for the grippotyphosa and bataviæ infections the icterus percentage is low, but the absolute figures are small.

With regard to the other clinical symptoms, I have no exact figures to offer, and I can only state that just as icterus may appear among patients infected with any of the serological *Leptospira* types, so also do the other symptoms characteristic of the classical Weil's disease appear in patients infected with the other types, though generally in a smaller degree. On principle, therefore, the clinical observations are inadequate to the determination in each individual case of the cause of the infection.

Before entering on the epidemiological facts, I shall mention some results obtained from examinations made on animals. These examinations mainly concerned rats, dogs, and mice.

In 1934, Zuelzer, examining 93 rats, found 23 *Leptospira* carriers. In 4 of these carriers the *Leptospiras* excreted were avirulent to guinea-pigs. It does not appear that these avirulent *Leptospiras* were submitted to serological examination, but the virulent ones were sero-

logically *L. icterohæmorrhagiæ*. About 1940, Ottosen, at the State Veterinary Serum Laboratory, examined 685 rats, and from 33% of these he cultivated *Leptospiras* from the kidneys. 112 of the isolated strains were inoculated in guinea-pigs and 18 of these, i.e. 16%, proved to be avirulent, although serologically 14 of these strains were *icterohæmorrhagiæ* (the remaining 4 were not submitted to serological examination). Among 16 strains isolated by me from 67 rats I did not come across any such avirulent strains. All were *L. icterohæmorrhagiæ* and all virulent to guinea-pigs.

From dogs in Denmark *L. icterohæmorrhagiæ* and *L. canicola* have been cultivated. *Leptospirosis canicularis* is most prevalent among the dogs in Copenhagen and in the large provincial towns, mainly occurring in the autumn months. During the period of 1943-45 it actually became epizootic. Since then the prevalence has decreased considerably. In the rural districts infection with *L. icterohæmorrhagiæ* appears to be the more prevalent. In 1937, in one village, 53 dogs were examined and 19 of them found to have positive sero-reactions. Only one of these showed a strong reaction for *L. canicola* and the remaining 18 for *L. icterohæmorrhagiæ*; *Leptospiras* were discovered in only two of the dogs. In dogs, excretion of *Leptospiras* has been seen to continue for several months. Usually, however, it is of shorter duration; in a considerable number of seropositive dogs *Leptospiras* were not discovered in the urine.

Investigations on mice were commenced in 1939, as in many instances epidemiological information from *L. sejroe* patients seemed to preclude rats as the source of infection, whereas the evidence pointed to mice as the most probable source. The first mouse to be examined was a harvest mouse (*Mus musculus spicilegus*) from a farm where one case of *L. sejroe* had occurred. This mouse had *L. sejroe* in the kidneys. A total number of 164 harvest mice from various parts of the country have been examined. From the kidneys of 18 of these mice *Leptospiras* were isolated. Of the 18 strains 16 were *L. sejroe*. The 17th strain could not be identified with any of the known *Leptospira* types, wherefore, in 1944, it was described as a special type: *L. ballum*. The 18th strain, isolated from the harvest mice, was serologically identical with two strains previously isolated from 2 out of 8 big wood mice (*Apodemus flavicollis*). These strains represent another serological type, *L. saxkoebing*, which is, however, closely related to the *sejroe* type. Of 123 voles (*Microtus arvalis*) 29 carried *L. grippotyphosa*, while 32 of another vole species (*Microtus agrestis*) proved negative.

To recapitulate: From mice we have isolated 4 different serological types of *Leptospiras*, viz.: *L. sejroe* and *L. ballum* from harvest mice, *L. saxkoebing* from harvest mice and wood mice, and *L. grippotyphosa* from voles.

Animal species other than the ones already mentioned have been investigated only inadequately, and no conclusive results were obtained.

*L. bataviæ* and *L. poi* have not been isolated in Denmark either from man or animal, but regarding the other types there is good agreement between the findings already made in animals and the information available from many of the patients with reference to the probable source of infection. These findings, moreover, afford a natural explanation of the distribution of the various infections in man with regard to seasons, sex, and occupations.

Fig. 1 shows the monthly distribution of cases of the various *Leptospira* infections, covering the fourteen years 1935-48. It is a matter of 780 cases, viz. 240 *icterohæmorrhagiæ*, 95 *canicola*, 414 *sejroe*, 15 *grippotyphosa*, and 16 *bataviæ*. In the graphs all the five curves show a level part and a peak.

The *L. sejroe* infections show a rise in the curve in August, reaching a maximum in October, and again returning to level in January. It is interesting to note that practically all the cases of *L. sejroe* infection were among the rural population, and that the harvest time in Denmark is in August and the first part of September. The harvest mice, which keep to the fields in the spring and summer seasons, follow the grain crop to the farms, and since the harvest mice are carriers of the *sejroe* type, it is easily understood why the incidence of human infections accumulates during the months of August-December.

If curves are made for men and women separately it is seen that while the curve for men begins to rise in August, the curve for women does not begin to rise until September. This shows clearly that in the case of women the infection takes place mainly in the farmhouses.

To this I may add that in 1943 an unusually great number of mice appeared in Denmark resulting, as might be expected, in a very great number of *sejroe* cases in the same year, as you see in Table I.

The peak of the curve for the *grippotyphosa* infections is much flatter than that of the *sejroe* infections, and the maximum is in August, i.e. in the beginning of the harvest season. This may be explained by the fact that the voles, the carriers of the *grippotyphosa* type, unlike the harvest mice, remain on the fields and do not go to the farms. Correspondingly



all the instances of grippotyphosa infection in Denmark have occurred among rural people in males, who in Denmark do the main field work. All the cases occurred in Jutland and mostly in South Jutland. This incidence corresponds to the dispersion of the grippotyphosa-harboring species of the voles (*arvalis*). This species is most prolific in South Jutland, with a decrease in density towards the northern part of Jutland; it does not exist in the Danish islands. Also the incidence of grippotyphosa infections was at its highest peak in the "mouse-year" 1943.

The curve for the bataviæ infections is almost coincident with the grippotyphosa curve, the maximum of the peak being reached in September; still, instances of bataviæ infection may appear also at other seasons. As in the case of the grippotyphosa infections, all the bataviæ infections occurred among rural males in Jutland. As previously said, the bataviæ type has not been found in animals in Denmark. We have yet to investigate the pigmy mouse (*Mus minutus*) proved by Mino to be a carrier of the *L. bataviæ* in Italy. However, the fact that the prevalence of bataviæ infections during the "mouse-year" of 1943 was not excessive might indicate that in Denmark mice are not carriers of the bataviæ type.

The incidence of canicola infection piles up during the months of October-December, corresponding to the prevalence in the autumn of canicola-infected dogs. Almost half of the number of canicola patients are women; which is in agreement with the fact that it is usually women who take care of ailing dogs and mop up their excreta.

For the greater prevalence of icterohæmorrhagiæ infections during the last half of the year I can offer no explanation. In Denmark, as in most other countries, the victims of icterohæmorrhagiæ attacks are pre-eminently men. More than one-half of the cases are

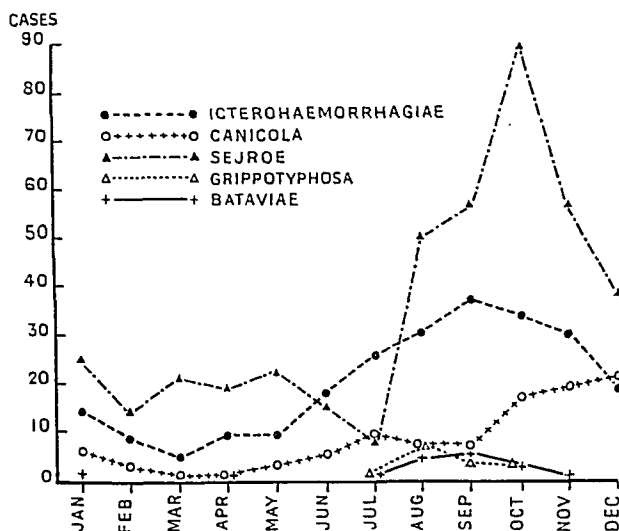


FIG. 1.

rural. In the towns, butchers appear to be the most exposed, those employed in this occupation alone accounting for about one-fifth of the icterohæmorrhagiæ infections among men in the urban districts.

I now propose to make some remarks on the bacteriological diagnosis of leptospirosis.

The ideal diagnosis consists of course in the isolation and determination of the *Leptospiras* in each single case. For a classification of the cultivated *Leptospiras* we have relied upon their antigenic properties. Morphologically all *Leptospiras* are alike, and cultural methods to distinguish pathogenic *Leptospiras* have not yet been found. The virulence is not a stable quality, as it usually decreases quickly when the *Leptospiras* grow *in vitro*. Moreover, for the determination of virulence we introduce another changeable factor, namely the power of resistance of the experimental animal. The antigenic properties of the *Leptospiras*, on the other hand, show a very high degree of stability. Therefore, we have identified new strains by serological comparison with those previously known, using cross-absorption tests in strains showing similarity to one another. This is how in 1938 we were forced to conclude that *L. sejroe* was a new serological type. And later in the same way we have had to describe

*L. saxkoebing* and *L. ballum* as new serological types. In this way also we distinguished the two types of *L. icterohæmorrhagicæ*, named A and AB. The great majority of icterohæmorrhagicæ strains isolated in Denmark could be classified as one of these two types, but two strains, one from a man and one from a rat, were not serologically identical with either of these two types, neither were they identical one with the other.

Similar results have been obtained in other countries, and there is no doubt that by application of the cross-absorption test to the numerous strains which are now being isolated all over the world we shall finish up with a very considerable number of serological types in the strict sense of this word.

In practical diagnostic work we can isolate the *Leptospiras* from only a minority of cases. For the rest we must be content with the microscopical demonstration of *Leptospiras* in the urine or we must rely on the demonstration of specific antibodies.

In routine work we cannot, of course, use strains of all serological types for our serum test. We must confine ourselves to the use of strains of such types as are known from the cultivation experiments to occur in the area in question, and perhaps a few others, the occurrence of which we want especially to investigate.

On the basis of seroreactions alone it is not always easy to decide the serological type of the infection of the patient, as the sera mostly react with strains of several types. Generally we may reckon that the strain which gives the strongest reaction corresponds to the one which has caused the infection of the patient, but in the first few weeks of the disease it is not uncommon that heterologous reactions are stronger than homologous reactions. However, if the antibody content in the serum of the patient can be followed during a sufficiently long time, the homologous reaction will finally be the dominating one.

But it is also possible that all the observed reactions are actually co-reactions, namely in such cases where the infection is caused by *Leptospiras* of a serological type which is related to, but not serologically identical with, any of the strains used for the seroreaction.

Therefore, in connexion with material from patients like that dealt with in the first part of this paper, it is really not correct to speak of infection of different types, it would be more correct to say that we have here been dealing with infections of different serological groups.

#### REFERENCES

- BORG-PETERSEN, C. (1938) *Acta convent. III de trop. morb. Amsterdam*, 1, 396.  
 — (1944) *Acta path. microbiol. scand.*, 21, 165, 504.  
 —, and JACOBSEN, E. (1937) *C. R. Soc. Biol. Paris*, 126, 799.  
 OTTOSEN, H. E. (1939) *Maanedsskr. Dyrleg.*, 51, 15.  
 — (1941) *Maanedsskr. Dyrleg.*, 53, 173.  
 ZUELZER, M. (1935) *Acta path. microbiol. scand.*, 12, 511.

**Dr. J. C. Broom:** The first human case in England of infection with *L. canicola* was reported by Baber and Stuart in 1946. In 1947 Dr. Alston and I confirmed the diagnosis in 3 cases, and during 1948 we had no less than 14. There is no reason to suppose that the infection rate in dogs has been increasing, so it is likely that human cases occurred in earlier years but were not diagnosed; many cases may still be going unrecognized.

Although the disease presents no pathognomonic symptom, the clinical picture is fairly typical when viewed as a whole, and closely resembles other benign forms of leptospirosis. The disease generally runs a mild course, but severe nephritis sometimes develops. In Bukh's case (1940) the blood urea rose to 280 mg.%, and the urinary output fell to 25 ml. a day. The patient was critically ill but he finally recovered.

One fatal case occurred in England last year, in a woman who suffered from chronic nephritis. Albuminuria and oliguria persisted during the 2nd apyrexial stage. The blood urea reached 500 mg.%, anuria supervened, and the patient died of uræmia. Details of this case have been published in the *Lancet* by Weetch, Colquhoun and Broom. We know of one other fatal case in Holland. No report has yet been published but Professor Ruys and Professor Wolff told me that polycystic disease of the kidneys was found at autopsy. The presence of pre-existing kidney damage may thus gravely prejudice the patient's chance of recovery in a severe attack.

In this country only *L. icterohæmorrhagicæ* and *L. canicola* have been found to cause human infections. We have tested serum from a number of patients presenting signs of aseptic meningitis against *L. grippotyphosa*, *L. pomona*, *L. bataviæ* and *L. sejroe*, but invariably with negative results.

The rodent carriers of these species are present in England, but no adequate surveys have

been undertaken so far to determine whether they are infected. The only evidence I know is contained in a paper by Elton *et al.* (1931) who were investigating the ecology of a colony of wood mice (*Apodemus sylvaticus*). Leptospiras were seen in the kidneys of 29 mice, but injection of the material into guinea-pigs produced only one infection, and that strain was not cultivated. With present knowledge and facilities, however, such a survey might lead to more definite results.

#### REFERENCES

- BABER, M. D., and STUART, R. D. (1946) *Lancet* (ii), 594.  
 BUKH, N. (1940) *Ugeskr. Læg.*, 102, 1142.  
 ELTON, C., FORD, E. B., BAKER, J. R., and GARDNER, A. D. (1931) *Proc. zool. Soc. Lond.*, p. 657.  
 WEETCH, R. S., COLQUHOUN, J., and BROOM, J. C. (1949) *Lancet* (i), 906.

Dr. R. D. Stuart (Glasgow) described briefly the observations made by Mr. I. McIntyre (Royal Dick Veterinary College, Edinburgh) and himself on canine leptospirosis. The high incidence of *L. canicola* infections and their specific relationship to canine renal disease had been adequately determined in the examination of 270 dogs. Serological evidence of this type of leptospirosis was found in 90% of 130 dogs with detectable renal disease, but only in 23% of 140 other dogs. A raised blood urea was accepted as unequivocal evidence of renal disease, and the specificity of the *L. canicola* agglutinins was confirmed by the isolation of the organism from blood culture in a number of cases. An attempt had then been made to outline the course of *L. canicola* disease in dogs in relation to pathogenesis and clinical findings. It was suggested that the disease process could be divided into the following stages:

(1) *Invasive*.—The stage of leptospiral infection of the blood stream, identifiable by blood culture.

(2) *Primary renal* when signs of renal damage first appeared. It followed about one or two weeks after the primary invasive stage and was identified by a high serum titre to leptospiræ, a raised blood urea and usually leptospiruria.

(3) *Secondary renal*.—This followed at a variable interval, sometimes weeks, sometimes years, after the primary renal stage, and was generally associated with a recurrence of renal symptoms. It was due to the persistence and progression of renal damage after animals had recovered from leptospiral infections. Thus it was often associated with a low serum titre for leptospiræ and a high blood urea but leptospiræ were never found in the urine.

*Leptospira canicola* infections also occurred in humans. The illness was often mild and featureless and consequently was extremely difficult to diagnose clinically. On one occasion Mr. McIntyre was able to suggest that the owner of one of his canicola-infected dogs had herself been suffering from the same disease. This was confirmed serologically. It seemed possible, therefore, that veterinary workers who had the opportunity of observing what was a fairly characteristic disease in dogs might be in a very good position to assist their medical colleagues by drawing attention to the possible ætiology of some obscure febrile process in the owners of infected animals.

Mr. H. I. Field (Institute of Animal Pathology, Cambridge): Members may be interested to know that we have recently diagnosed *Leptospira* infection in a 14-day-old Aberdeen Angus calf. The animal died after a five-day illness characterized by an initial temperature of 105° F., dullness, inappetence, salivation and a brownish discoloration under the tongue. An intense icterus developed during the twenty-four hours preceding death. The history on the farm suggested that calves had died previously of the same type of infection. Some supporting evidence that the affected calf was not an isolated case of *Leptospira* infection was obtained later. Subsequent to the diagnosis being established another calf on the same farm showing similar symptoms made a dramatic recovery following the injection of *L. icterohæmorrhagiæ* hyperimmune serum.

There is no record to show that *Leptospira* infection has been diagnosed in cattle previously in this country, yet it may be regarded as surprising, if the calf is naturally susceptible, that the disease does not occur frequently in view of the high incidence of rats in and around farm buildings. We have isolated *Leptospira* from trapped rats on the farm on which the clinical case occurred, and while this in itself does not prove that rats acted as the source of infection to the calves, it does at least show that a potential source of infection was present on the farm.

*Leptospira* infection of cattle has been reported from Russia, Palestine and the U.S.A., but the strains isolated appear to be distinct antigenically from *L. icterohæmorrhagiæ*.

The examination of the strain isolated by us is not completed but there is every reason to believe from the preliminary observations that it is a virulent strain of *L. icterohæmorrhagiae*.

Dr. J. T. Edwards (London) said he had been much struck by the statements made by Drs. Borg-Petersen and Stuart. He recalled his own early experiences at the Pathological Department of the Royal Veterinary College, London, where the lesions of "small white kidney" (chronic interstitial nephritis) and "enlarged white kidney" (chronic fatty infiltration) were observed to be exceedingly common in the adults of the dog and cat species, respectively; he had always been under the impression that these conditions arose through some as yet undisclosed metabolic disorder. That both types of lesion could arise through a common disorder of that kind was now evident from the address given recently before that Section by Professor Himsworth (*Proc. Roy. Soc. Med.*, 1949, 42, 201) dealing with liver damage of metabolic origin. Now, however, Dr. Stuart had supplied data that would lead one to suspect that the canine disorder, at any rate, could be attributed, in its proximate origin, to a specific infective process, namely leptospirosis, in view of the disclosures made of the unsuspected widespread prevalence of that infection among dogs. Dr. Borg-Petersen, in his investigations upon the prevalence of the same infection among animals, had also related its discovery in cats. He would like to know from him whether he could give some more precise information regarding its prevalence in that species. That a specific infection of this kind could precipitate the onset of pathological states which had all the appearances of metabolic disturbances was, of course, quite possible. The information now forthcoming was teaching them to be wary of ascribing the proximate cause of such states to idiopathic faulty metabolism until every precaution had been taken to exclude the possibility of a specific infection. Many alleged disorders in the human subject which had been attributed in the past to a great variety of idiopathic disturbances had been traced through the surveys of Dairymple-Champneys (*Public Health*, 1948, 61, 239) to be essentially sequels of chronic brucellosis. These afforded yet another lesson of the kind in the realm of comparative medicine.

Dr. C. Borg-Petersen (Copenhagen), in reply: Information regarding feline leptospirosis in Denmark is very scanty. In a cat with jaundice and pulmonary hæmorrhages Ottosen found a positive seroreaction with *L. icterohæmorrhagiae* 1 : 1,000, but cultivation experiments and guinea-pig inoculation were negative. In 7 other cats the results were entirely negative.

In relation to the findings of Dr. Stuart and Mr. McIntyre in dogs in Edinburgh it might be of interest to mention some very similar results from Copenhagen: By histological examination of the kidneys from 197 stray dogs Mr. Ottosen found chronic interstitial nephritis in 45 dogs; of these 45 dogs 36, or 80%, were seropositive. Of the 152 dogs without nephritis only 19, or 13%, were seropositive.

## Section of the History of Medicine

President—E. ASHWORTH UNDERWOOD, M.A., M.D., D.P.H.

[March 2, 1949]

### The History of Research upon the Renal Circulation<sup>1</sup>

By K. J. FRANKLIN, D.M., F.R.C.P.

*Department of Physiology, St. Bartholomew's Hospital Medical College, London*

#### Introductory

At the outset, it may help if I adapt a more general statement (Franklin, 1948) to the special circumstances of this lecture, and say that studies of the renal blood circulation should have as their primary objective the acquisition of knowledge about the intact and un-anæsthetized human being and lower animals at various stages (pre-natal as well as post-natal) of their lives, under all conditions from rest to maximal activity, and over a wide range of variations in external environment (these two last clauses refer mainly to post-natal). The knowledge required is as follows:

(1) How, in what amount, at what speed, and at what pressure the blood is distributed to the kidney.

(2) Details relating to its passage through the various parts of the organ, or to its by-passing of them.

(3) Data about its passage from the peripheral parts to the renal vein.

As subsidiary objectives, of medical and veterinary importance, I can add the above, as affected by:

(a) Disordered conditions of the body.

(b) Narcotics and/or anæsthetics.

(c) The administration of other substances by various routes.

(d) Hæmorrhage at varying rates and of various total amount.

(e) Surgical procedures, and allied interventions.

(f) The transfusion of blood or of blood components.

The above is, I think, reasonably comprehensive as regards the renal *blood circulation*. In order, however, to appreciate any purposive character which that circulation may exhibit, we should also know what changes in composition and in amount the blood undergoes during its passage through the kidney, and what are the destinations and functions and so forth of the materials separated from, and added to, the blood during that passage.

I have already mentioned so much, and suggested to you so many obvious gaps in our knowledge, that I hesitate to add to the list. I must, however, point out that the renal blood circulation cannot be fully described without complete knowledge of the renal vascular system and its innervation, for as Claude Bernard (1937) wrote—*anatomy localizes physiology*. Not only personal observations, but also those recorded in past and recent literature, point to the fact that there is still very much, even in these more anatomical fields, which remains to be revealed.

#### Vesalius to Johannes Müller

It is with the above ideal attainment of knowledge in mind that I ask you for a while this afternoon to slip back into the past and to review some of the contributions made by our predecessors. I will begin with Vesalius' views on the kidney (Foster, 1901). Amply supplied with both veins and arteries, its substance, he wrote, strains off from the venous and arterial blood some but not all of the serosity. He was, however, at a loss to explain how the straining was effected. Next, I wish to pay a passing tribute to Lorenzo Bellini who in 1662, at the age of 19, published his short tract in which the uriniferous tubules, as seen by the naked eye, were first described. Guided by his master, Borelli, Bellini expounded a physical theory of the production of urine. "The minute arteries", he wrote, "discharge their contents into spaces in the kidney parenchyma, whence the aqueous serosity of the blood presses into the beginnings of the urinary canaliculi, while the rest of the blood finds its way out by the veins. The selection of the one path and of the other is determined by the size and configuration of the particles; those of the aqueous serosity fit into the canals of the canaliculi, those of the rest of the blood do not" (Foster, 1901).

<sup>1</sup>An abridged and somewhat amended version of the account given to the Section of the History of Medicine at its meeting on March 2, 1949. In the time available it was impossible to do more than survey a few major tendencies. I hope, however, to produce a fuller account at some future date for publication in *Ann. Sci.* or elsewhere.—K. J. F.

Four years after Bellini, i.e. in 1666, Marcello Malpighi published his account of the kidney and went far beyond the former. He regarded the cortex as composed of rounded internal renal glands (the Malpighian corpuscles) attached to the ends of the small arterial twigs like bunches of apples to the branches of a tree. At the surface and more internally, they were interposed between the urinary ducts, and they could be injected from the arterial side with ease, from the venous side with some difficulty. Their connexion with the uriniferous tubules was not so distinct, but Malpighi appears to have regarded the glands as sites for the elaboration of urine, which passed into the ducts.

After Malpighi, Ruysch (1701, 1702, 1703) injected the vessels of kidneys and his work needs a word or two of explanation, which I will borrow from Cole (1944). Galen and the ancients believed that there were parts of the body which had no vascular supply. Ruysch, by achieving the injection of ever finer and finer vessels, established the ubiquity of the blood vascular system, but at the same time strengthened a view which originated with Erasistratus in the sixth century B.C., that the tissues were but vascular networks, variously arranged. In this depreciation of the part played by the parenchyma, the importance attached to glandular tissues decreased, and the diverse activities of the tissues were explained on the individualities of their vascular supplies. "Malpighi, who had rightly understood the relations of glandular tissue and blood supply, was thus opposed and thrust aside by Ruysch and his followers, who denied the very existence of glandular tissue, and could see in a gland nothing but a subtle complex of blood capillaries."<sup>2</sup>

In addition, some of the substances (water, mercury, tallow, wax, air) injected by Ruysch and others (including, according to von Haller, Eustachius and, according to Bowman, Albinus) into the renal arteries came out through the urinary ducts of the papillæ, even though the veins had not been ligated. The various possible explanations of this happening need not, perhaps, concern us here, except that we may dismiss that particular one according to which exhalant arteries with open stomata opened directly into the excretory canals. In 1778, however, von Haller stressed the injection findings rather than Malpighi's more fundamental contribution, and von Haller's authority was such that we can imagine the resultant pause in progress.<sup>3</sup> Four years later, in 1782, Schumlansky continued the discussion about the connexion between corpuscles and uriniferous tubes, and he was followed by Huschke (1828) and by Johannes Müller (1830), who denied a connexion.

The latter, in his work on the more intimate structure and the development of the secreting glands, gave a great many details about the comparative anatomy of the kidney—we may remember that such comparative structural study was, at the time, perhaps the main basis of physiological ideas. Müller noted the occurrence of Malpighian corpuscles or receptacles in frogs, toads, tortoises, birds, mammals, and man, and their absence from crocodiles, serpents, and fishes. He described them as rounded bodies, with a cavity vesicular and bloody, occurring in the cortex of the kidney and distinguishable, on the one hand from the larger arterial twigs, on the other from the blood-vascular network lying between the urinary ducts. He stressed the separateness of the ducts from the blood-vessels, and was at a loss to suggest a function for the corpuscles. Solly, who epitomized Müller's findings in an English publication in 1839, suggested that they might merely act as diverticula to the blood when it was not employed in secretion, just as the spleen (it was supposed) did in relation to the organs of digestion.

The standard English textbook of the time was Herbert Mayo's *Outlines of Human Physiology*, and in the fourth edition, which appeared in 1837, is the following account of the kidney. "Its artery, termed the renal or emulgent, is, relatively to the size of the gland, the largest in the body": it readily transmits injected fluids into the emulgent veins and excretory tubes. The renal nerves are derived from the semilunar ganglia or solar plexus; several small ganglia are formed upon them: when the renal nerves are divided in a dog, the animal expresses pain.<sup>4</sup> By making a section from the external convex edge of the kidney

<sup>2</sup>That Ruysch had some justification is evident from the modern investigations made by Shonyo and Mann (1944) during their neoprene injections of the renal vascular tree. They stated, with respect to the normal kidney, that "the ease with which neoprene is injected and the extent of the cast make it possible to demonstrate the extreme vascularity of the kidney, a fact which is not so readily appreciated by studies on histologic sections and the usual injection-corrosion specimens. In completely injected specimens the vascular tree is so dense that grossly the corroded kidney appears to be almost as solid as does the uncorroded one (figs. 1 and 2)."

<sup>3</sup>In the same volume he collected details about the renal vessels, e.g. he noted Senac's (1749) postulate, based on anatomical measurements, that the kidneys receive somewhat less than a sixth of the total aortic blood flow.

<sup>4</sup>*Cf.* details of the amount of the renal blood flow given later in this article.

<sup>5</sup>This early indication of the presence of afferent fibres in the renal nerves is corroborated by personal experience in the anesthetized animal, and is of considerable significance in modern views of kidney functioning.

through to the internal concave edge, the different substances of which the gland is composed are displayed. The outer or cortical part is of a granulated texture, but seems after a successful injection to consist of tortuous vessels alone; processes of the same substance extend towards the concavity of the kidney, between which are contained cones of what seem white convergent fibres . . . the white fibres are excretory tubes, which have their origin in the cortical substance; the mode of their connexion with the blood-vessels has not been ascertained. While immersed in the cortical part, that is to say near their origin, the excretory tubes are highly tortuous: in the white cones their course is straight."

At about the same time as this statement was made by the Senior Surgeon of the Middlesex Hospital, George Corfe, resident medical officer thereof, published a popular treatise on the kidney (1839). As this was quoted at some length by Solly in the volume in which he epitomized Müller's findings, it is of interest to see what views could be expressed without exciting comment! Corfe stated that the urine was separated by the kidney, but denied that this "excrementitious drain" could derive from the "life-giving blood" which the renal artery brought to the organ. His own view was that the urine is a secretion *from oil and venous blood*.<sup>6</sup>

It is a pleasure to turn from Corfe's statements to a second account by Johannes Müller which was published in 1839 and reads: "*The disposition of the blood-vessels in the substance of the kidney* is extremely interesting. In the cortical structure they form the ordinary capillary network, of which the meshes are so close that the intervals are not many times larger than the diameter of the capillaries that enclose them. Among the tubuli uriniferi of the cortical substance lie the acini of Malpighi, bodies larger than the urinary canals, (see the table of measurements,) and visible even with the naked eye. Schumlansky has drawn them much too small. They lie in vesicular cavities of the cellular tissue between the tubuli uriniferi, and consist wholly of convoluted blood-vessels. It is remarkable that they exist in the kidneys of most, perhaps all, vertebrate animals; they have been found in the kidney of the frog, toad, salamander, turtle, and tortoise, birds, mammalia, and man [and recently by Hyrtl in the kidney of fishes]. Schumlansky first advanced the hypothesis that these *glomeruli* are the source of the urinary secretion,—that the tubuli uriniferi take their rise in them. The more accurate examinations of Huschke and myself, however, have shown that such is not the case, for the glomeruli or corpora Malpighiana can be injected only from the arteries, never from the secreting canals. In the salamander, too, Huschke has seen the blood-vessel, which enters each of the glomeruli, issue from it again, after having made numerous convolutions. They can be filled with injection from the arteries as easily as from the veins,<sup>7</sup> and are simply receptacles for blood.

"The convoluted tubuli uriniferi themselves are the seat of the secretion of urine, which is poured out by their whole internal surface, not by their extremities only. They are everywhere surrounded by minute currents of blood, circulating in the capillary network which fills their interstices, and is extended over their external surface. The fluid part of the blood may permeate the delicate parietes of the uriniferous canals, and suffer in its transit a chemical change; or the effete matters contained in the blood of the capillaries may be attracted and separated from it by the agency of those canals.

"In the medullary portions of the kidney the blood-vessels run between the urinary canals in straight lines, from the cortical portion towards the mammella. These straight blood-vessels are easily injected either from the arteries or the veins, and were formerly supposed to be urinary canals, and to prove the existence of a communication between the blood-vessels and ducts of glands. But they differ from the secreting canals in becoming smaller as they approach the mammella, on which they terminate in the common capillary network which surrounds the openings of the tubuli uriniferi."

The work of Müller and his pupils, e.g. Schleiden, Henle and Schwann, like that of Wharton Jones, Sharpey, Todd, Paget, Gulliver and Goodsir in our own country, was in no small measure made possible by the improved compound microscope which came into use about 1830; the related enunciation of the "cell doctrine" by Schwann in 1839 was an event of the utmost importance.

<sup>6</sup>In Corfe's day, as earlier, experimental physiology was largely lacking and deductions from anatomy could not usually be checked. Hypotheses were rife and chance factors, not fitness, determined their survival, as one can see in another field, namely, the history of ideas about the fetal circulation (Franklin, 1944).

<sup>7</sup>Translator's comment: "This expression seems to imply that the glomeruli may be filled with injection from the veins; but the translator cannot find a statement to that effect in the writings of any of the modern anatomists who have studied the structure of the kidneys; and he is informed both by Mr. Owen and by Mr. Kiernan, that in their minute injections of these organs they have never seen the matter thrown into the veins pass into the bodies in question."

### William Bowman (1816-1892)

William Bowman, whose contribution to renal vascular studies and to ideas of renal physiology appeared in 1842, had earlier assisted Dr. Blakiston, to whom he had been apprenticed in Birmingham, in certain cardiac researches and in gratitude for this help Blakiston had presented him with a compound microscope. Few gifts to youth can ever have been more fruitful! During those apprentice years, also, Bowman exhibited great manipulative skill and powers of draughtsmanship. In 1837, at the age of 21, he went to King's College, London, where Robert Bentley Todd, aged 28, was the recently appointed Professor of Physiology and of general and morbid Anatomy. In the next year Bowman became his demonstrator, and the long partnership between the two men began, Todd contributing (Keith, 1930) enthusiasm and daring, Bowman cool judgment and technical skill. Todd's monumental *Cyclopædia of Anatomy and Physiology* was already under way (vol. 1 had appeared in 1835-6, vol. 2 was in press), and he enlisted Bowman's help with the future volumes, as well as with the contemplated *Physiological Anatomy and Physiology of Man*, of which they later became joint-authors. Bowman, as the one to be responsible for dealing with the micro-structure of skin, sense organs, nerves, lining membrane of the alimentary canal, glands, lungs, liver, kidneys, testes, voluntary and involuntary muscles, bone and cartilage, decided to investigate for himself rather than to derive from the German histologists, and in consequence his papers on muscle, the kidney, &c. were accounts of research results obtained during the course of work primarily undertaken in connexion with the production of an encyclopædia and a textbook. For the paper on muscle he was elected F.R.S., for that on the kidney he was given a Royal Medal, and he was still only 27 years old when he received the second honour.

The 1842 article was entitled "On the structure and use of the Malpighian bodies of the kidney, with observations on the circulation through that gland". In it Bowman stated that the uriniferous tubes consist of an external *basement membrane* (his term) lined by epithelium, and that the Malpighian body (in man and various lower animals) is a rounded mass of minute vessels invested by a cyst or capsule of precisely similar appearance to the basement membrane of the tubes, and continuous with the latter. The relationship had previously been missed because it is only directly opposite the points of entry of the vas afferens and exit of the vas efferens that the orifice of the uriniferous tube is apparent. The beginning of the tube in the frog exhibits ciliated epithelium in activity.

Bowman's idea of the renal circulation, based on his structural findings, was that "All the blood of the renal artery (with the exception of the small quantity distributed to the capsule, surrounding fat, and the coats of the larger vessels) enters the capillary tufts of the Malpighian bodies; thence it passes into the capillary plexus surrounding the uriniferous tubes, and it finally leaves the organ through the branches of the renal vein". Incidentally, he noted the larger size of the deeper [basal or juxtamedullary] glomeruli, their wide efferent vessels, the branching of each of these latter into several vessels of appreciable calibre which passed inward towards the pelvis, with venous return vessels running, in similar fashion, more or less parallel with the uriniferous tubes of the medulla.

From the arterial side, the Malpighian tufts could be readily injected and, with less freedom, the capillaries surrounding the uriniferous tubes. The capillaries, but not the tufts or the arteries, could be injected from the venous side. If the vessels ruptured, the uriniferous tubes might become injected from either the arterial or the venous side. From the uriniferous tubes, without extravasation, it was impossible to inject the Malpighian bodies, the peritubular plexus, or the veins.

Much else of interest in Bowman's article must, for reasons of space, be omitted from this present account, but we should refer briefly to his views of the function of the glomeruli. He believed that water passed from the blood via the glomerular vessels and dissolved, in its passage along the uriniferous tube, the secretions of the epithelial cells of that tube. Diuretic medicines, he thought, acted specially on the Malpighian bodies and various foreign substances, particularly salts, which, when introduced into the blood, pass off by the urine with great freedom, exuded in all probability through this bare system of capillaries. They also appeared to be the likely route of escape, in pathological cases, of sugar, albumen, and the red particles of the blood.

### 1842 Onwards

From 1842 onwards it is difficult to produce a brief and, at the same time, interesting story if one follows chronologically the course of the findings as a whole. I propose, therefore, from this point to follow a number of individual lines, in succession, up to modern times.

(1) *Theories of renal secretion*.—After Bowman's filtration-secretion theory of 1842 came Carl Ludwig's filtration-reabsorption one of 1844, which appeared to be supported in 1854 by the work of Goll, who showed that the urine flow was closely related to the arterial pressure. On the other hand, many vascular effects and also points in regard to the blood-urine



concentrations were left unexplained. In 1870, also, Ustimovitsch showed that administration of urea would re-start urine secretion which had stopped through fall of arterial pressure, so Ludwig conceded that blood composition, as well as blood-pressure, was involved. Then, in 1874, R. Heidenhain and, in 1878, Nussbaum reported the results of experiments which appeared to support Bowman's theory. After a long break, in 1917, Cushny produced his modern theory, according to which filtration of plasma less colloids occurred in the glomeruli, and reabsorption of a modified Ringer-Locke solution occurred in the tubules. The thesis was derived from a very critical review of the literature rather than from personal experiments, and its main achievement, apart from a severe purge of previous publications, was probably the stimulus it gave to A. N. Richards, who began his beautiful work with Wearn in 1922, and, by direct methods, produced some definite facts about the processes occurring in the frog's kidney. Subsequently, E. K. Marshall, jr., added to knowledge of secretory processes and produced valuable suggestions from comparative anatomy. Finally, renal clearance tests, in which Van Slyke, Rehberg, Homer Smith and others have been concerned, have added much to our knowledge. At the present time, it is generally held that the mammalian vasculo-nephritic unit exhibits filtration through the glomerulus and reabsorption through the tubules, but that in specific instances tubular secretion also occurs.

(2) *The renal vascular system.*—Under this heading there is much to record, but I will confine myself to a few points:

(a) The greater size of the mammalian basal glomeruli, their wide vasa efferentia, and the continuation of these latter, after the giving off of a few capillaries, as leashes of vasa recta passing towards the pelvis and thereafter returning from it were, even if incompletely, described by Bowman and pictured by Frey. In recent times, they received more thoroughgoing attention from Lee-Brown in 1924, and from the Nuffield Institute team, particularly—on the microscopical aspect—from Daniel and Prichard, in 1946–47. There was a functional directive in this latter case for the further anatomical work, for it had been found that the blood flow by-passed, under a variety of experimental circumstances, some or all of the cortical glomeruli (*see Trueta et al., 1947*).

(b) From 1847 onwards, there have been descriptions in the literature of arteriovenous connexions which by-pass the glomeruli. The detailed findings over about a century are given by Clara (1938) and by Shonyo and Mann (1944). Clara admitted:

(i) Branches from vasa afferentia which pass straight to the peritubular capillary network (Ludwig's branches). They are few in number but not necessarily, for that reason, unimportant.

(ii) Terminal branches of the interlobular arteries which make connexions in all degrees (up to being recognizable perforating arteries) with capsular vessels.

(iii) An adipose capsular artery which can arise from the aorta, or from the renal artery, or from the spermatic artery (the adipose capsule can also receive branches from the lumbar, suprarenal, and phrenic arteries). From the adipose capsule the fibrous capsule is supplied, and the capsular and cortical capillary networks have connexions. So the tubules can get blood when the glomeruli are cut off from the blood circulation. On the other hand, such a supply cannot for long be at all adequate for anything other than maintenance of the tubular tissues.

(iv) *Arteriae rectae* vere passing from the arcuate arteries into the medulla.<sup>a</sup>

(v) Arteriovenous anastomoses which were perhaps first noticed in the kidney by Gross (1868). In the human kidney, according to Spanner (1937), they occur to the number of 360 per sq. cm. in the sinus renalis, arising from branches of interlobar arteries; in the cortex at all levels, either between interlobular arteries and veins, or between interlobular arteries and branches of stellate veins; in the capsular region, to the number of 264 per sq. cm., from the interlobular-capsular arterial network to stellate or cortical veins.

Shonyo and Mann (1944), who used neoprene injections, reported as follows:

"Various possibilities have been recorded in regard to the various short circuits in renal circulation. The present trend is to accept such vessels as occurring in pathologic specimens only, and they are considered to be either absent or extremely rare in normal kidneys. The results of the present investigation indicate that such shunts probably do occur regularly in the normal renal circulation of several species of animals, and the following have been observed: (1) direct continuations of the interlobular arteries into the capillaries of the cortex corticis; (2) vessels which by-pass glomeruli in the corticomedullary zone and pass into the medullary capillaries; (3) direct arteriovenous shunts in the corticomedullary zone."

<sup>a</sup>According to Landois and Stirling (1891), these constitute the larger part of the vessels supplying the medulla and, in contradistinction to the vasa efferentia of the basal glomeruli, have muscular walls. Because of their supposition about the number of these vessels, Landois and Stirling considered the circulation through the vasa recta to be most important, regarding it as forming a side stream or "short-cut" through which much of the blood might pass without traversing the cortical vessels. Each such medullary branch of the arcuate artery was stated to break up into a leash or pencil of small arterioles, i.e. to behave in similar fashion to the vasa efferentia of a basal glomerulus.

At least two further sources of information are available. First, the late Dr. A. E. Barclay (personal communication 26.1.49), as a result of his microradiographic studies, thought that the medullary vascular loops arising from the vasa efferentia of basal glomeruli were comparatively rare, while direct anastomoses in the arcuate zone were common. He also found various other types of arteriovenous connexions, and regarded the whole problem as by no means finally solved.<sup>9</sup> Secondly, Simkin *et al.* (1948) injected glass spheres 80–400 $\mu$  in diameter into human autopsy kidneys and into the renal arteries of live dogs, and found, though precautions were taken to exclude capsular by-passes, that some of the spheres passed through the kidneys. Obviously, some fairly wide anastomotic channels were present.

Personal experience, in experiments on living rabbits, inclines me also to think that diversion of the cortical blood flow is not, on all occasions, or *in toto*, via vasa recta. On the other hand, I should like to see Spanner's findings tested by independent observers, for the number of anastomoses recorded by him is phenomenal, if correct, and their importance is obviously related to the frequency of their occurrence.

(3) *The renal blood-pressure.*—In 1847 Ludwig added a float to Poiseuille's hemodynamometer, "had the genius to cause this float to write on a recording cylinder, and thus at one coup gave us the kymograph, or wave-writer, and the application of the graphic method to physiology" (Stirling). The attraction, and the comparative ease, of recording arterial pressure by such means led to a great amount of work, and Claude Bernard, according to his posthumous publications (1937), thought physiologists were being diverted from more fundamental things.

"The circulation," he wrote, "on which I shall discourse this year, is encumbered by an unparalleled mass of experimental work and needs to be freed from such encumbrance. There have been dissertations on instrumental methods and upon the absolute blood-pressure. All this is without significance and disappears in face of the discovery of the vasomotor nerves. One must get away from all the trivialities and go for a few typical, classical experiments, performed under exacting conditions." Somewhat similarly, Jarisch wrote in 1928 that "For the development of the knowledge of the circulation it was certainly unfortunate that the amount of the blood flow is relatively so difficult, and the blood-pressure relatively so easy, to measure. In consequence, the blood-pressure manometer exerted an immediate fascination, though it is blood in quantity rather than blood under pressure that most organs require."

The kidney, however, as we know, is an organ that requires blood not only in quantity but also under pressure, and the blood-pressure has long been conceded to be of prime importance in urine formation. Its measurement in the vasa efferentia and the glomerular capillaries has been effected, I believe, only in the frog. In this species, in 1927, Hayman found systolic pressures in the aorta and vas afferens to be about 29 and 24 mm.Hg respectively, while the diastolic in the glomerular capillaries was 15 to 16 mm.Hg. In the mammal, by less direct methods, it has been calculated that the glomerular pressure may be 70 mm.Hg when the general arterial pressure is 130 mm.Hg (Winton and Bayliss, 1948).

(4) *The speed of the blood flow* in the main renal artery and vein is of less obvious interest than the intrarenal circuit time, which in the intact, anesthetized rabbit averages about 2.5 sec. (Trueta *et al.*, 1947). This figure may be compared with 2.7 sec. for the pulmonary circuit in the mature sheep foetus (weighing about 5 kg.) before functional closure of the ductus arteriosus and 1.4 sec. after such closure (Barclay *et al.*, 1942), or with the figure of 2 to 5 sec. found by Robb and Steinberg (1940) for the pulmonary circuit time in adult man. All the above times were radiographically determined, and all are surprisingly fast.

(5) *The amount of the blood flow.*—We have already noted Senac's 1749 estimate of this. In 1867 Ludwig introduced his Stromuhr, and in 1891 it was modified by Tigerstedt; soon thereafter Hürthle introduced his recording Stromuhr. Such apparatus, however, require severance of continuity of the vessels into which they are introduced, so they need not concern us except as historical instruments. Barcroft and Brodie (1904, 1905) measured the renal flow by a different technique (timing with a stop-watch the passage of 10 ml. blood into a tube introduced into the dog's renal vein) but in many ways their experimental animals were unlike normal intact ones, e.g. they had been in large measure eviscerated. We know now, also, that the renal blood flow is particularly susceptible to manipulation of neighbouring parts. The introduction by Rein in 1928 of his Thermostromuhr overcame some of the objections valid against the earlier types of Stromuhr, and in 1932 Glaser, Laszlo and Schürmeyer, continuing work begun in co-operation with Rein and Eppinger, reported flows of 0.5 to 7.2 ml. per gramme kidney tissue per minute in dogs, with the majority of readings between 1 and 4 ml. p.g.p.m. The amounts represented an appreciable part of the heart-minute-volume, but were not directly related to it or to the blood-pressure. There were, however, direct relationships between amount of blood flow, oxygen usage and carbon dioxide production, i.e. the authors concluded that the renal blood flow regulation is an

<sup>9</sup>Further details will doubtless be found in his posthumous book. Oxford: Blackwell Scientific Publications Ltd. (In the press.)

autonomic function of the organ itself. The desaturation of the arterial blood within the kidney, as noted by earlier observers from Claude Bernard onwards, was slight.

In 1933 Medes and Herrick reported blood flows in dogs which had undergone unilateral nephrectomy, had had a Thermoströmuhr applied to the remaining renal artery, and had been studied after recovery. The renal flows in these animals ranged from about 10 to 24 ml. per kg. body-weight per minute.

In 1936, in his *Introduction to Human Physiology*, Rein stated that 1,500 litres per day (just over 1 litre p.m.) was not an overestimate of the human renal blood flow. In 1938, Clara gave the average p.m. as  $3.5 \times$  the weight of the kidney (each human one weighs approximately 130 grammes), or the total flow through both organs as 0.7 to 1.4 litres p.m., i.e. about as much as through the two lower extremities, and a considerable fraction of the heart-minute-volume.

These estimates were validated in 1939–40 and subsequently, when Homer Smith and his associates used diodrast plasma clearances at low plasma concentrations as a guide, and determined the effective renal blood flow in adult man as about 1,300 ml. p.m. or more than a quarter of the heart-minute-volume. We may as well add here that each human kidney has over 1,000,000 glomeruli, that the glomerular filtration rate, as determined by inulin clearance, was given by Homer Smith as 131 ml. p.m., that this filtration occurs through nearly 1 sq. m. of glomerular capillary surface area, and that of the 131 ml. only 1 ml. is excreted in the urine, the other 130 being reabsorbed by the tubules.

Homer Smith's comment (1943) was as follows: "Examining the pattern of the human kidney, we must not be surprised to find that it is far from a perfect organ. In fact, it is in many respects grossly inefficient. It begins its task by pouring some 125 c.c. of water into the tubules each minute, demanding for this extravagant filtration one quarter of all the blood put out by the heart. Out of this stream of water, 99 per cent must be reabsorbed again. This circuitous method of operation is peculiar, to say the least. At one end, the heart is working hard to pump a large quantity of water out of the body; at the other end the tubules are working equally hard to defeat the heart by keeping 99 per cent of this water from escaping. Thus heart and kidney are literally pitched in constant battle against each other—our lives depend on neither one of them ever winning out . . . In consequence of the circuitous pattern of the filtration and reabsorption of water, nearly half a pound of glucose and over three pounds of sodium chloride per day, not to mention quantities of phosphate, amino acids and other substances, must be saved from being lost in the urine by being reabsorbed from the tubular stream. There is enough waste motion here to bankrupt any economic system—other than a natural one, for Nature is the only artificer who does not need to count the cost by which she achieves her ends."

According to Janssen and Rein (1927), however, the kidney is one of the organs which need very large blood flows to prevent their temperature from rising unduly.

(6) *Intermittence of the glomerular blood flow.*—The concept that the degree of glomerular activity of the whole kidney is susceptible to adjustment through increase or decrease in the number of active glomerular units was stated as early as 1859 by Hermann, a colleague of Ludwig, but was first clearly demonstrated—in the frog—by Richards (see Richards, 1925). I myself recall a very beautiful microfilm of the frog's kidney made by Dr. Alfred Jäger of Bonn. In the resting state only a few glomeruli were visible, but very quickly after an injection of caffeine double the number could be seen. In the mammal some or all of the cortical glomeruli can be reflexly (Trueta *et al.*, 1947) or humorally (Theobald and Verney, 1935; Rydin and Verney, 1938) put off duty for varying lengths of time, and (see evidence in Richards, 1925) albuminuria may occur on restoration of the blood flow in consequence of the previous vasoconstriction.

(7) *Occurrence of red streamlines in the renal vein.*—As early as 1849 Claude Bernard noted such red streamlines but he did not publish until 1858 and 1859, when he was primarily concerned with the salivary glands. He considered that the venous blood showed up red when the kidney was in full activity, as was the case with the salivary glands. Gas analyses showed how little oxygen had been lost by the blood in its intrarenal passage. Incidentally, this work of Bernard in 1849 was, I believe, the first *experimental* work on the renal circulation. In 1875, three years before Bernard's death, Vulpian published further observations on the red streams in the renal veins.

Thereafter, the phenomenon seems to have vanished from the ken of physiologists and others until 1936, when McLachlin and I reported red streamlines in a variety of veins, including the renal ones. We thought we had discovered something new and no one at the Meeting of the Physiological Society, at which we demonstrated our findings, made any comment to the contrary. In 1938 Clara reverted to Bernard's findings as possible evidence of the activity of arteriovenous anastomoses.

In 1945-47 the streamlines became associated in the minds of Trueta *et al.* with diversion of blood from the renal cortex, and on more than one occasion pulsation was observed in the renal vein blood.

(8) *The oncometer*.—The first renal oncometer was designed under strange circumstances, according to Sir Charles Sherrington (personal communication, 1934). C. S. Roy qualified at the age of 21, and soon thereafter, in 1876, went to act as a military surgeon in the Turkish Army during the war with Serbia. While stationed in Anatolia, he lived in a whitewashed hut and had little to do. So he drew the initial designs for the oncometer on the whitewashed wall of his hut. Later, he completed the apparatus and in 1883 published, with Cohnheim, results attained by its use. Thereafter, it was employed by Bradford and countless others in kidney research. Its drawback, from our present point of view, is that the volume changes recorded include not only those of blood content, but also those of urine and lymph.

(9) *The nervous control of the renal blood flow*.—There is plenty of evidence that, before the nineteenth century, an action of the nerves on the blood-vessels was appreciated (e.g. it was so by Jenner). But 1840 was a year of special significance, for in it Henle announced the finding of smooth muscle fibres in the media of arteries, and Stilling not only coined the term "vasomotor", but gave a surprisingly full and accurate, if theoretical, account of the vasomotor system. Thereafter it was not unduly long before discoveries about the vasomotor nerves began to be made and, so far as the kidney is concerned, the first published observations were those of Goll in 1854; he found vasoconstriction on stimulation of the cord. From then on the number of publications has been very great, both with regard to stimulation of effector nerves and also with regard to reflexes affecting the renal blood flow. One of the best-known papers is that of Bradford (1889), but many others which are much less well known are worthy of study.

I cannot, in the time at my disposal, review the whole of this vast field, but I can make a few comments. In the first place, in the earlier part of our period, animals, like man himself, were operated on without anaesthesia and while, in retrospect, we must deplore the pain inflicted, especially in experiments involving the use of curare, it is possible to glean from the protocols information which cannot now, under modern vivisection conditions, be obtained. I think we owe it to these animals of the past to make full search for any useful knowledge obtained through their suffering, e.g. stimulation of the afferent splanchnic fibres was noted to be painful.

Secondly, in the earlier nerve-stimulation work, galvanization was used where now we mostly use faradic stimuli. So here again we may profit by careful study of the literature. Bradford, too, found that he could produce vasodilatation by a slow rate of stimulation, while vasoconstriction resulted from a more rapid rate, and this lead might with profit be pursued farther.

Claude Bernard envisaged in secretory glands a double blood flow designed to respond to the different conditions introduced by the intermittent activity of the glands. Beside the local capillary circulation with its on and off periods, the anastomotic routes, he wrote, provide a passage for the blood when the gland is physiologically at rest. In this latter condition the blood circulates through more direct routes, like a crowd traversing the streets without entering the houses which line them. Of these two circulations, the one, by the direct routes, is continuous and mechanical; the other, the capillary functional one, is intermittent. It is on this second one in particular, he wrote, that the nervous system exerts its influence.

I need not say much about the numerous vasoconstriction findings on distal splanchnic stimulation or stimulation of the renal nerves themselves, or about the vasodilator effects of section of these nerves, or about the reflex vasoconstriction which can be produced in the kidney from a variety of receptor fields. For these are well known, and lists of references are given by McDowall (1938) and others. I should like, however, to note that Vulpian's (1875) accounts are of considerable interest, and that the résumé given by Foster (1877) in his textbook shows how much had already been accomplished by that date. In recent times one of the more interesting findings has been the suggestion that the blood flow can be diverted from the renal cortex in consequence of stimulation of the supraorbital surface of the frontal lobe. Joseph Cort, who produced this suggestion as a result of research done while he was a student at Yale, used Evans Blue as an indicator of the renal blood diversion, and this technique has since been criticized. So he proposes (personal communication, 1949) to verify his findings, using such criteria as changes in blood gas composition within the renal vein. Other brain centres which by their activity affect the renal blood flow are being investigated (personal communication, 1948) by Hess and his co-workers in Zürich.<sup>10</sup> Finally,

<sup>10</sup> While this paper has been in the press, Hoff *et al.* (1949) have reported interesting results of cerebral stimulation, and McGee and Ullmann, in my own Department, have determined the spinal segments which control anoxic and hypercapnic diversion of the renal cortical blood flow when higher parts of the nervous system are out of action.

it is important to note the findings of Verney *et al.*, who have found that the nervously produced liberation of adrenal medullary and post-pituitary hormones can produce vasoconstriction within the denervated kidney. In this field, therefore, as in others, both the nervous and the hormonal effects have to be borne in mind in accounting for the local reactions of the kidney vessels, and the effects of these reactions upon the renal blood flow, under a variety of physiological circumstances.

### Concluding Remarks

In a review of this length it has been impossible to cover adequately all aspects of the subject, and I have also felt at liberty, in an Address to the Section of the History of Medicine, to amplify certain earlier and less well-known parts of the story. I have deliberately omitted reference to the relation between intrarenal phenomena and hypertension, partly because of the limits of space, partly because research has not "advanced to the point at which conclusive answers to questions can be given" (Shorr, 1948), partly because the subject, in its present state, ought properly to be reviewed by someone with more specialized knowledge than I can claim.

Perhaps, however, I have been able to convey some idea of the very great progress achieved, in the past century or so, in respect of knowledge of the renal blood flow and its regulation. Perhaps, too, this relation of past achievement may be a stimulus to further research. If it is so, the review will have been well worth while, for impaired renal functioning is the greatest single cause of fatalities and disablements in the medical field to-day, and in consequence a successful piece of renal research may have unusually widespread application in the prevention and treatment of disease.

I close with acknowledgments to my various renal research colleagues, in particular to Professors Josep Trueta, E. C. Amoroso and W. C. W. Nixon, to Mr. John Sophian, and to members of my Department at St. Bartholomew's Hospital Medical College.

### REFERENCES

- BARCLAY, A. E., BARCROFT, J., BARRON, D. H., FRANKLIN, K. J., and PRICHARD, M. M. L. (1942) *J. Physiol.*, **101**, 375.
- BARCROFT, J., and BRODIE, T. G. (1904) *J. Physiol.*, **32**, 18.
- , — (1905) *J. Physiol.*, **33**, 32.
- BELLINI, L. (1662) *Exercitatio anatomica de structura et usu renum*. Florentiae.
- BERNARD, C. (1858a) *Leçons sur la physiologie et la pathologie du système nerveux*. Paris.
- (1858b, c, d) *C.R. Acad. Sci., Paris*, **46**, 159, **47**, 245, 393.
- (1859) *Leçons sur les propriétés physiologiques et les altérations pathologiques des liquides de l'organisme*. Paris.
- (1937) *Pensées. Notes détachées*. Paris, pp. 46, 57.
- BOWMAN, W. (1842) (See also KEITH, A., 1930.) *Philos. Trans.*, **132**, 57. Reprinted in *The Collected Papers of Sir W. Bowman, Bart., F.R.S.*, ed. by J. Burdon-Sanderson and J. W. Hulke, 1892, **1**. London.
- BRADFORD, J. R. (1889) *J. Physiol.*, **10**, 358.
- CLARA, M. (1938) *Arch. Kreislaufforsch.*, **3**, 42.
- COHNHEIM, J., and ROY, C. S. (1883) *Virchows Arch.*, **92**, 424.
- COLE, F. J. (1944) *A History of Comparative Anatomy from Aristotle to the Eighteenth Century*. London, pp. 306, 308.
- CORFÉ, G. (1839) *A Popular Treatise on the Kidney: Its Hitherto Unknown Functions and its Diseases, in Connection with the Circulating Animal Oils, &c. With Advice to Persons on Their Secretions*. London.
- CUSHNY, A. R. (1917) *The Secretion of Urine*. London.
- FOSTER, M. (1877) *A Text Book of Physiology*. London.
- (1901) *Lectures on the History of Physiology During the Sixteenth, Seventeenth and Eighteenth Centuries*. Cambridge, pp. 102, 110.
- FRANKLIN, K. J. (1944) Chapter I of *The Fetal Circulation and Cardiovascular System, and the Changes That They Undergo at Birth*, by A. E. Barclay, K. J. Franklin, and M. M. L. Prichard. Oxford.
- (1948) *St. Bart's Hosp. J.*, **52**, 27.
- , and McLACHLIN, A. D. (1936) *J. Physiol.*, **86**, 386, **88**, 263.
- GLASER, H., LASZLO, D., and SCHÜRMEYER, A. (1932) *Arch. exp. Path. Pharmacol.*, **167**, 292.
- GOLL, F. (1854) *Z. rat. Med.*, n.f., **4**, 78.
- GROSS, C. F. (1868) *Essai sur la structure microscopique du rein*. Strasbourg, Paris, Genève.
- HALLER, A. von (1778) *Elementa physiologiae corporis humani*, **7**, 2nd Edn., Liber xxvi, Sectio I. Rens, eorumque fabrica. Lausannæ.
- HAYMAN, J. M., jr. (1927) *Amer. J. Physiol.*, **79**, 389.
- HEIDENHAIN, R. (1874) *Pflüg. Arch. ges. Physiol.*, **9**, 1.
- (1875) See note on p. 576 of *Elements of Human Physiology*, by D. L. Hermann, transl. from the 5th Edn. by Arthur Gamgee. London.
- HERMANN, W. (1859) *S.B. Akad. Wiss. Wien, math. naturw. Kl.*, **36**, 358. Quoted.
- HOFF, E. C., KELL, J. F., jr., HASTINGS, N., GRAY, E. H., and SHOLES, D. M. (1949) *Federation Proc.*, **8**, 435.
- HUSCHKE (1828) See Müller, J. (1839).
- HYRTL (1838) See Müller, J. (1839).

- JANSSEN, S., and REIN, H. (1927) *Ber. ges. Physiol.*, 42, 567.
- JARISCH, A. (1928) *Dtsch. med. Wschr.*, 54, 1171, 1211.
- JENNER, E. See Baron, J. (1838) The Life of Edward Jenner, M.D., LL.D., F.R.S., 1, 93-94. London.
- KEITH, A. (1930) *Brit. med. J.* (i), 701.
- LANDOIS, L. (1891) A Text-book of Human Physiology, Including Histology and Microscopical Anatomy; With Special Reference to the Requirements of Practical Medicine. Transl. from the 7th German Edn. With additions by W. Stirling. Fourth Edn., London, 1, 485.
- LEE-BROWN, R. K. (1924) *Arch. Surg., Chicago*, 8, 831.
- LUDWIG, C. (1843) Beiträge zur Lehre vom Mechanismus der Harnsekretion. Inaug. Diss., Marburg. Quoted.
- (1844) Nieren und Harnbereitung, pp. 628-640 in Handwörterbuch der Physiologie, mit Rücksicht auf physiologische Pathologie, ... herausgegeben von Dr. Rudolph Wagner, 2. Braunschweig.
- (1861) Nieren, pp. 373-434 in Lehrbuch der Physiologie des Menschen, 2nd Edn., 2. Leipzig und Heidelberg.
- (1871) Von der Niere, pp. 489-507 in Handbuch der Lehre von den Geweben des Menschen und der Thiere, ... herausgegeben von S. Stricker, 1. Leipzig.
- MCDOWALL, R. J. S. (1938) The Control of the Circulation of the Blood. London, New York, Toronto.
- MALPIGHI, M. (1666) De renibus, pp. 71-100 in De viscerum structura exercitatio anatomica. Bononiae.
- MARSHALL, E. K., jr. (1926) *Physiol. Rev.*, 6, 440.
- (1934) *Physiol. Rev.*, 14, 133.
- MAYO, H. (1937) Outlines of Human Physiology, 4th Edn. London.
- MEDES, G., and HERRICK, J. F. (1933) *Proc. Soc. exp. Biol., N.Y.*, 31, 116.
- MÖLLER, E., McINTOSH, J. F. and VAN SLYKE, D. D. (1928) *J. Clin. Invest.*, 6, 427.
- MÜLLER, J. (1830) De penitiori structura renum, Liber decimus, pp. 84-102 in De glandularum secretorum structura penitiori earumque prima formatione in homine atque animalibus. Commentatio anatomica Cum tabulis aeri incisus xvii. Lipsiae.
- (1839) Elements of Physiology, transl. by W. Baly, 2nd Edn., 1, 494. London.
- NUSSBAUM, M. (1878) *Pflüg. Arch. ges. Physiol.*, 16, 139, 17, 580.
- REHBERG, P. B. (1929) *Zbl. inn. Med.*, 50, 367.
- REIN, H. (1928) *Z. Biol.*, 87, 394.
- (1936) Einführung in die Physiologie des Menschen. Berlin.
- RICHARDS, A. N. (1925) *Amer. J. med. Sci.*, 170, 781.
- and WEARN, J. T. (1923) Demonstration to XI International Congress of Physiologists, Edinburgh. (See also Wearn, J. T., and Richards, A. N., 1924.)
- ROBB, G. P., and STEINBERG, I. (1940) *J. Amer. med. Ass.*, 114, 474.
- ROY, C. S. For biographical details see Who Was Who 1897-1915, London; and Rolleston, H. D. (1932) The Cambridge Medical School. A Biographical History. Cambridge.
- RUYSCH, F. (1701) Thesaurus anatomicus primus. Amsterdam. Asser secundus. No. VIII, 4.
- (1702) Thesaurus anatomicus secundus. Amsterdam. Asser sextus. No. I.
- (1703) Thesaurus anatomicus tertius. Amsterdam. Asser secundus. No. XLI.
- RYDIN, H., and VERNEY, E. B. (1938) *Quart. J. exp. Physiol.*, 27, 343.
- SCHUMLANSKY (1782) See Müller, J. (1839).
- SENAC, J. B. (1749) Traité de la structure du cœur, de son action, & de ses maladies. Paris.
- SHONYO, E. S., and MANN, F. C. (1944) *Arch. Path., Chicago*, 38, 287.
- SHORR, E. (1948) *Amer. J. Med.*, 5, 783.
- SIMKIN, B., BERGMAN, H. C., SILVER, H., and PRINZMETAL, M. (1948) *Arch. intern. Med.*, 81, 115.
- SMITH, H. W. (1943) Lectures on the Kidney. Lawrence, Kansas, pp. 19-20.
- SOLLY, S. (1839) The Intimate Structure of Secreting Glands. By John Müller, M.D. ... With the Subsequent Discoveries of Other Authors. London.
- SPANNER, R. (1937) *Klin. Wschr.*, 16, 1421.
- STILLING, B. (1840) Physiologische, pathologische und medicinisch-practische Untersuchungen über die Spinal-Irritation. Leipzig.
- STIRLING, W. (1895) *Med. Chron. Manch.*, n.s., 3, 178.
- THEOBALD, G. W. (1934) *J. Physiol.*, 81, 243.
- and VERNEY, E. B. (1935) *J. Physiol.*, 83, 341.
- TODD, R. B. (1835-59) The Cyclopaedia of Anatomy and Physiology, ed. by R. B. Todd. London.
- and BOWMAN, W. (1856) The Physiological Anatomy and Physiology of Man, 2. London.
- TRUETA, J., BARCLAY, A. E., DANIEL, P. M., FRANKLIN, K. J., and PRICHARD, M. M. L. (1947) Studies of the Renal Circulation. Oxford.
- USTIMOVITCH (1870a) *Arb. physiol. Anst., Leipzig*, 5, 199. Quoted from Stirling, W. (1895).
- (1870b) *Ber. sächs. Ges. (Akad.) Wiss., math. phys. Cl.*, 22, 430. Quoted from Cushny, A. R. (1917).
- VAN SLYKE, D. D., McINTOSH, J. F., MÖLLER, E., HANNON, R. R., and JOHNSTON, C. (1930) *J. clin. Invest.*, 8, 357. See also Möller et al. (1928).
- VERNEY, E. B. (1946) *Lancet* (ii), 739, 781.
- (1947) *Proc. roy. Soc., B*, 135, 25.
- (1948) *Brit. med. J.* (ii), 119.
- VULPIAN, A. (1875) Leçons sur l'appareil vaso-moteur (physiologie et pathologie) faites à la Faculté de Médecine de Paris. Paris.
- WEARN, J. T., and RICHARDS, A. N. (1924) *Amer. J. Physiol.*, 71, 209.
- WINTON, F. R., and BAYLISS, L. E. (1948) Human Physiology, 3rd Ed. London, pp. 252-5.

## Section of Physical Medicine

President—L. C. HILL, M.D., F.R.C.P.

[April 13, 1949]

### DISCUSSION ON THE SIGNIFICANCE OF PATHOLOGICAL TESTS IN RHEUMATIC DISEASE

**Dr. Douglas H. Collins:** There is a regrettable tendency in many branches of Medicine, and certainly not least in rheumatology, to requisition numerous tests on each patient in order to display activity and interest in his case. It may be cynically remarked that the pathological tests to which patients on their admission to hospital or clinic are submitted fall into two categories—"diagnostic tests" and just "tests". To these two categories must be added a third, which affects the patient a little later in his career and which may conveniently be termed "progress tests", finding out, for instance, the sedimentation rate in the control of rheumatism or tuberculosis and the prothrombin time in anticoagulant therapy.

Before ordering any test to be performed on the patient, the clinician should ask himself: "Is it significant? Do I stand a reasonable chance of getting a clear answer? Do I really want to know the answer?"

For my own part I want to start the Discussion by referring to the contribution that the histologist or cytologist can make to the diagnosis and management of the rheumatic patient, or rather of the patient who presents himself in the rheumatism clinic, for, apart from the everyday run of typical varieties of rheumatic disease, atypical cases and instances even of rare disease make their almost daily appearance in the large rheumatism centre, which necessarily has to be competent in the diagnosis of all manner of medical and surgical conditions manifesting themselves as disorders of the locomotor system. The investigations to which I shall refer require the removal of material by aspiration or excision biopsy and are naturally not applicable in all cases, but, where they can be employed, direct information about the underlying pathological processes can generally be obtained and these examinations, therefore, fall into the category of diagnostic or significant pathological tests.

**Synovial effusions.**—It is, of course, imperative that an acute effusion in an acutely inflamed joint, except in a clear case of rheumatic fever, should be withdrawn and examined, since the early and correct diagnosis of suppurative arthritis is vital. Such fluid ought to be collected in three containers, one a dry sterile vessel for the specimen to be sent to the bacteriologist for culture and for testing of penicillin or sulphonamide sensitivity of any organisms recovered. The second portion of the fluid, in an oxalated tube to prevent clotting, is for the total and differential cell count. This cell count is made in the ordinary W.B.C. pipette but using normal saline as a diluent instead of weak acetic acid, since acetic acid precipitates mucin. The third specimen should be kept in a plain tube to observe the formation of clots. After subsequent centrifuging, smears or sections of the cell deposit may be made, and the overlying fluid tested for blood or bile pigment. These are the three examinations which give all the information ordinarily required in examining a joint fluid: bacteriological culture and smears, cytology and the examination for blood and blood derivatives.

Septic arthritis can be identified by the presence of pus and organisms. Rheumatoid arthritis can be differentiated from osteo-arthritis because the leucocyte count in the first is of the order of 20,000 and in the second of the order of 2,000 cells per c.mm. Traumatic effusions always contain either blood, or blood pigments, depending upon the period elapsed since the trauma was sustained. Many investigations have been made on the mucin content of synovial effusions. Although it is generally the case that the mucin content and the viscosity of the effusion are reduced in all forms of inflammatory arthritis, the examination is of little use in diagnostic differentiation since the mucin concentration varies very widely through the amount of watery exudate with which it is mixed.

The high proportion of neutrophil polymorphs in the effusion of rheumatoid arthritis seems rather surprising in view of the preponderance of lymphocytes in the synovial membrane in this disease. It can, however, be explained. Detailed examination of the synovial tissues in rheumatoid arthritis always shows a small number of polymorphs. These cells enter the tissues from the blood-vessels, as do the lymphocytes, but, possessing greater motility, and possibly responding to chemotactic influences, they more readily work their way through the synovial lining and enter the joint fluid, becoming relatively concentrated there.

*Biopsy of synovial tissues.*—Most of the biopsy specimens of synovial tissue that I have examined have come from the orthopaedic departments and I am impressed by the frequency with which positive help has been given in the diagnosis and management of the patient by this method of examination. I know that many cases pass through rheumatism clinics in which this examination would be valuable, and that in certain clinics in America it is used much more extensively than it is used in this country.

A man of 37 had had a chronic effusion of the left knee-joint for four years. Synovial biopsy showed heavy siderosis of the stratum synoviale. No diagnosis had been reached by previous aspirations although blood derivatives had been present. Neither the history nor the radiology had led to a diagnosis. The biopsy shows that this was a chronic hæmarthrosis, and subsequent synovectomy revealed a diffuse, cavernous, synovial hæmangioma. Four years of physiotherapy had been wasted on this patient.

Repeated hæmarthroses should also lead to a detailed hæmatological examination. Thrombocytopenic purpura, leukæmia and, more often, hæmophilia may be the cause of the intra-articular bleeding. I sometimes wonder how often this last condition fails to be diagnosed. Hæmophilia is not a very rare disease, and 80% or more of hæmophiliacs suffer hæmarthroses (in knee, elbow, ankle or elsewhere). 60% develop chronic joint disease which is, in effect, a secondary osteo-arthritis (Thomas, 1936). Recently together in the children's ward of the Leeds General Infirmary there were two boys with hæmophilic arthritis. The first knew his own diagnosis and worried little about his disability except on account of the pain whenever a joint became acutely distended with blood. The second had had his first hæmorrhage into one hip-joint, had been diagnosed as tuberculous coxitis, had been encased in a plaster spica and had lain unhappily in a sanatorium for months. He was transferred for further investigation because every time his B.S.R. was taken (which was always normal) he developed a huge hæmatoma on the arm. Even then the diagnosis was not suspected but was soon established by the revelation of a prolonged clotting time without other abnormality. The plaster was stripped off and he soon regained normal boyish vigour.

Synovial biopsy in suspected tuberculous arthritis is a routine examination in some orthopaedic departments. In the majority of instances a firm diagnosis can be made by the histologist. The method should be used in all cases of arthritis where the possibility of the tuberculosis exists, especially in monarticular disease. But it is worth while recalling that multiple tuberculous arthritis occasionally occurs. Ghormley and Brav (1933) found two joints affected in 13.1% and more than two joints in 5.4% of cases.

An extremely useful biopsy method for suspected tuberculous arthritis is the examination of a regional lymph gland. The results of this examination are not infallible, and occasionally false negative or, very rarely, false positive answers may be given, but it often gives strong support to a diagnosis of tuberculosis before X-ray changes are visible (Arden and Scott, 1947). The enlarged regional lymph glands in rheumatoid arthritis and Still's disease show only non-specific reactive hyperplasia:

I believe that a positive histological diagnosis of rheumatoid arthritis by synovial biopsy can almost always be made when the following features are together present: (1) hyperplasia of synovial membrane and villi; (2) hyperplasia of synovial lining cells; (3) massive lymphocyte or plasma cell infiltration of the sub-intima with large focal collections of these cells in the villi; (4) inflammatory hyperæmia and œdema varying in degree with the duration and intensity of the inflammatory processes; (5) absence of other specific histological features, for example, tubercle follicles or suppuration.



The histological diagnosis must, of course, be considered in relation with the clinical features. Experience teaches me that unless the five features just named are clearly recognizable in the sections, the diagnosis of rheumatoid arthritis cannot be justified. But even in the clinically atypical case when the rheumatoid picture is present, I believe the pathological diagnosis is true and that it has prognostic significance.

A synovial biopsy was made of a knee-joint in a man aged 29 with a monarticular arthritis thought by many surgeons to be tuberculous. On the strength of the histological report, the diagnosis of tuberculosis was abandoned, but a guarded prognosis was given which was justified by the follow-up two years later when the clinical condition of the joint was found to be unaltered, neither better nor worse. When the rheumatoid picture is identified in the biopsy, it is wise to predict that a chronic or subacute course of the disease in that joint will follow, and the possibility of other joints being subsequently involved cannot be excluded. This was the opinion expressed by Allison and Ghormley (1931), and I have been able to confirm it in several cases from whom I have had biopsies.

The synovial histology in osteo-arthritis is quite different. Villous proliferation on a small scale may be seen but the maximal leucocytic reaction is a few small, perivascular, lymphocyte foci.

*Tendon sheaths.*—Much the same remarks apply to the tendon sheaths as to the synovial membranes of joints. I believe that a rheumatoid tenosynovitis occurs. Cases of stenosing tenosynovitis show only cicatricial tissue without specific features. The identification of tuberculosis in some cases of compound palmar ganglion is often very difficult. The presence of rice bodies is thought always to indicate tuberculosis but I am doubtful about this. They certainly occur very often in tuberculous tendon sheaths, but these bodies may form by the desiccation of fibrinous exudate on the synovial surface in the absence of a caseous process. There is, of course, no doubt about the diagnosis of tuberculosis when the tendon sheaths are invaded by numerous hyperplastic follicles.

I am surprised how often the benign giant-cell synovioma of tendon sheaths fails to be diagnosed clinically. This small tumour, most often occurring in the flexor sheaths of the fingers, can be completely removed when small. Its histological appearance is characteristic. On at least three occasions I have known patients suffer for years because they were thought to be rheumatic nodules.

*Nodules.*—The structure of the rheumatoid subcutaneous nodule, when all features are taken into consideration, is quite characteristic. The focus of fibrinoid degeneration is not by itself the specific feature of the structure. A similar formation is seen in the dermis in granuloma annulare (Collins, 1939). The diagnosis of the rheumatoid nodule is certain when the whole lesion is examined. Except in the truly typical case of rheumatoid arthritis or rheumatic fever, the histology of all nodules should be examined. Amongst the conditions I have diagnosed from supposed rheumatic nodules were erythema nodosum, xanthoma multiplex, dermatofibroma, eosinophilic granuloma of skin, Hodgkin's disease and metastatic carcinoma. The fibrositic nodule is not identifiable histologically.

*Bone diseases causing rheumatic symptoms.*—Radiological diagnosis is to be relied on in most cases, but where there is doubt, laboratory help may be sought. The histological diagnosis of bone tumours is, of course, mainly a surgical problem, and the information to be gained from a study of the blood calcium, phosphorus and acid and alkaline phosphatase is widely known and lies outside the scope of this paper. In practice two laboratory methods of investigation give a great deal of help. In the case of an elderly patient with a painful spine and doubtful radiographic appearances, the diagnosis often rests between myelomatosis and carcinomatosis. In many cases of the former, a positive diagnosis can be reached by the identification of plasma cells or myeloma cells in sternal puncture material. In the latter repeated careful search of blood films may reveal a leuco-erythroblastic anaemia which strongly supports the diagnosis of osseous metastases. It should be remembered that skeletal metastases generally occur in the bones of the axial skeleton, i.e. those bones which in adult life contain red marrow, and that extensive deposits may be present in bone without causing an alteration of radiographic density, as Shackman and Harrison (1947-48) have so well illustrated.

#### REFERENCES

- ALLISON, N., and GHORMLEY, R. K. (1931) *Diagnosis in Joint Disease*. London.  
 ARDEN, G. P., and SCOTT, J. C. (1947) *Brit. med. J.* (ii), 87.  
 COLLINS, D. H. (1939) *Ann. rheum. Dis.*, 1, 38.  
 GHORMLEY, R. K., and BRAV, E. A. (1933) *Arch. Surg.*, 26, 465.  
 SHACKMAN, R., and HARRISON, C. V. (1947-48) *Brit. J. Surg.*, 35, 385.  
 THOMAS, H. B. (1936) *J. Bone Jt. Surg.*, 18, 140.

Dr. H. J. Gibson (Royal National Hospital for Rheumatic Diseases, Bath):

*Observations on the Relative Viscosity of Blood Plasma in Comparison with other Empirical Blood Tests on the Rheumatic Diseases*

During the past twenty years many tests have been described for the quantitative assessment of plasma abnormalities in the rheumatic diseases. They all depend on abnormal distributions of plasma proteins which are present in rheumatic arthritis, ankylosing spondylitis and gout and are absent or minimal in osteo-arthritis and fibrositis. The tests are all quite empirical and are not, as far as is known, related to the ætiology of the rheumatic diseases. They are negative in normal healthy subjects and show varying grades of abnormality in rheumatic diseases, the degree of deviation from normal showing some correlation with the apparent intensity or activity of the clinical disease. For this reason they may be used in the objective assessment of the results of treatment and as tests of cure or remission.

The B.S.R. is the test most frequently employed to-day; despite a lack of understanding of the precise mechanism underlying the test and the relatively crude methods of carrying it out its value in diagnosis is very great.

Its theoretical disadvantage is that the estimation of the essential plasma abnormalities is an indirect one through their effects on red-cell rouleaux formation and sedimentation in a glass tube. The rate of rouleaux formation is influenced by the concentration of red cells present and the rate of fall by the tube diameter used and probably also by factors related to the viscosity of the plasma/red-cell complex in relation to the inner surface of the tube. The fall of red cells in a narrow tube is accompanied by a rise of a corresponding volume of plasma. This flow of a complex colloidal mixture of proteins and intact cells may be profoundly influenced by the physical conditions existing at the glass surface. Houston *et al.* (1945) have shown in the case of plasma viscosity how different may be the results obtained in two tubes of apparently the same size and shape.

If a test could be found which could estimate directly the extent of plasma protein changes associated with tissue destruction then a considerable advance would have been made. Previous work has shown that these changes are very complex and that no simple estimation of fibrinogen, globulin and albumin will give the correlation with disease processes which the B.S.R. affords. More complicated methods of plasma protein study such as by electrophoresis are not practicable for routine tests on large numbers of cases.

The empirical tests to which I refer include, apart from the B.S.R., the formol-gel test which may be carried out on plasma or serum, the serum colloidal-gold test, the related thymol turbidity and flocculation tests, and the plasma viscosity. MacLagan (1948) has shown that the gold, thymol and formol-gel tests are indications of abnormalities of the globulins. Thus thymol and gold flocculation tests indicate an excess of gamma globulin. The gel tests are influenced by alpha, beta and gamma globulins and are closely correlated with the total globulin content. The plasma viscosity is probably also a measure of globulin increase although the results are modified by other proteins present.

The present communication records observations on the clinical application of the plasma viscosity in different forms of disease of the locomotor system and the correlation of the results with those of other empirical blood tests in these diseases. The method used is that of Woodmansey and Wilson (1948) to whom I am indebted for particulars of technique in advance of publication and for a sample tube with which our own might be compared.

The estimation of plasma viscosity as an objective index of abnormality in tuberculosis, rheumatism and other diseases has been reported by Miller and Whittington (1942), Houston and others (1945), Harkness and others (1946) and Cowan and Harkness (1947). In tuberculosis they have reported a high correlation between clinical activity and plasma viscosity. The only exception to this was seen in advanced cases before death when the state of "terminal decay" was associated with a diminishing viscosity. An interesting observation was a viscosity zone which was peculiarly associated with pleural effusions. In rheumatism Cowan and Harkness (1947) reported that plasma viscosity increases with progress of the disease in rheumatoid arthritis and decreases with improvement, the increase being proportional to the severity of the disease process. They classified their cases into four groups of (1) Residual deformity only, (2) Chronic, (3) Subacute, (4) Acute, and showed that the viscosity tended to fall into distinct zones corresponding to the clinical subdivisions. They stated that their results appeared to confirm that the viscosity is a more reliable index of the clinical condition than the B.S.R. If this proves to be correct then it is important that the test be introduced as a routine method replacing the B.S.R.

Study of their figures does not fully justify this conclusion in my opinion. Thus the group "residual deformity only" showed a raised B.S.R. by the Wintrobe method (average

19.8 mm. in one hour) which is in agreement with our experience. The "burnt out" case is now recognized to be very rare. In the series of 286 cases reviewed in this paper none was in this group although they included cases of up to forty years' duration. Evidence of activity was shown by clinical or histological examination in all. Cowan and Harkness (1947) found the average plasma kinematic viscosity in this "residual deformity" group to be within normal limits. The more active cases showed considerable discrepancies between B.S.R. and viscosity as indeed is only to be expected from the differing underlying mechanism of the test as emphasized by Race (1948). The evidence did not, however, appear to favour the viscosity as the more reliable index in every case. Thus their Case 4 showed *diminished* pain in joints following myocrisin and the B.S.R. was 40 mm. in one hour (Wintrobe). The

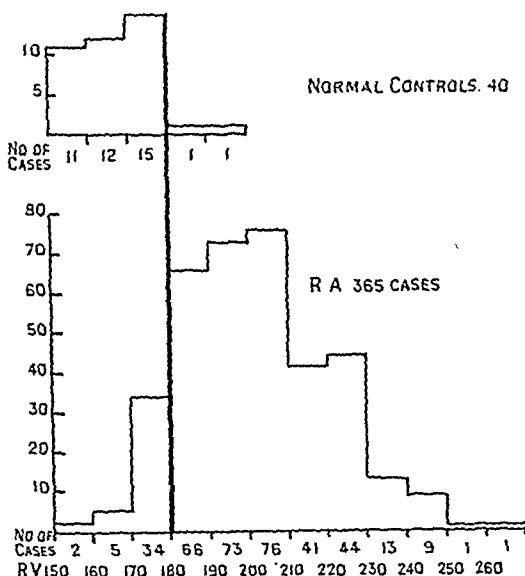


FIG. 1.—Relative viscosity. Rheumatoid arthritis and controls.

viscosity was within normal limits. The implication of the viscosity test that normality had been reached would appear to be unduly optimistic and most clinicians would be influenced by the rapid B.S.R.

At the same time the test was obviously one of considerable interest and steps were taken to test it in parallel with other plasma and serum reactions.

The makers could not at that time supply a viscometer of the Whittington type and the Harrogate method was used. The results cannot be compared directly with those of Cowan and Harkness for this reason. It is simply a measure of plasma viscosity relative to water. All tests, including those on controls, were made in the same viscometer at 20° C., undiluted oxalated plasma being used. The unit is the relative viscosity multiplied by 100. Normal is taken as from 150 to 180. Each result is the mean of three readings which always agreed very closely with one another. Replicate tests on the same plasma gave a high degree of consistency.

It is not proposed to discuss the physics of the test as this has already been done with great thoroughness by Houston, Harkness and Whittington (1945). Our aim is simply to present the results obtained in a series of normal healthy persons and of unselected cases as seen in a hospital for rheumatic diseases and to assess if possible the value of the test to the clinician.

## RESULTS

Relative Viscosity in the clinical types of rheumatic disease:

*Rheumatoid arthritis.*—Fig. 1 shows graphically the distribution of relative viscosity (R.V.) values in 365 observations made on 286 consecutive cases clinically diagnosed as rheumatoid arthritis (R.A.). For comparison the frequency distribution of 40 normal persons of similar age and sex is shown.

It will be seen that in both a sharp break occurs at the 180 line. That is, between the group 170–179 and 180–189. This agrees with the finding of Woodmansey and Wilson (1948) that the normal relative viscosity is 160–180 by the method used. 41 cases of R.A. showed a normal viscosity and 2 controls had a viscosity over 180. The controls in question were a physiotherapist and a ward sister who were apparently in excellent health and have remained so. The differentiation between cases and controls is therefore good but it will be noted that there is a tendency in both groups to show a maximum incidence in the viscosity ranges near the normal. While this is not necessarily a disadvantage in assessing progress in a case it means that a single estimation, on the average, may not give such clear diagnostic information as it would if the results in normal and abnormal groups were more widely spaced. It is probable that in any random sample of rheumatoid cases many results will be near the borderline of normality. This tendency can be seen in the kinematic viscosity results reported by Cowan and Harkness (1947) who showed that the mean value in 154 chronic rheumatoid arthritides was 2.121 units as compared with the upper limit of normal of 1.950.

*B.S.R. and viscosity in rheumatoid arthritis.*—In fig. 2 the corrected suspension stability (C.S.S.) as a measure of B.S.R. is shown graphically for the same series of cases and controls.

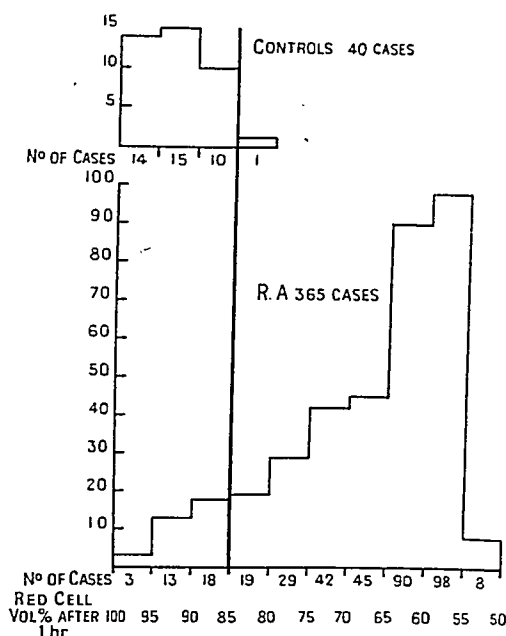


FIG. 2.—B.S.R. (C.S.S.) in rheumatoid arthritis and controls. Frequency distribution.

The normal controls show a peak incidence at 90–95% corresponding to a fall of 3–8 mm. in one hour; 25% of controls were in the group 85–90% which has always been regarded as normal. One control was in the 80–85% group, regarded as borderline.

The graph of frequency distribution in the case series shows in a striking way how markedly the B.S.R. (as estimated by the Spa Hospitals Method) is influenced in rheumatoid arthritis. It will be seen that the peaks of the curve are in groups far removed from the normal, in this respect contrasting with the viscosity distribution in the same series. In empirical tests of this kind in which an estimate is made of some ill-defined abnormality, their value both in diagnosis and in assessment of improvement or deterioration depends mainly on the extent of abnormality indicated and the differentiation which this estimate affords between diseased and normal persons. On this criterion the B.S.R. appears to be more informative than viscosity.

This conclusion is not invalidated by the occurrence of early packing when the B.S.R. is estimated by the short tube of the Spa Hospitals Method. The writer agrees with Race (1948) that differentiation within the most rapid B.S.R. groups (C.S.S. 55–65%) is not clearly

made by the tube in question. This is seen in the graph by the accumulation of large numbers of cases in these groups. This is not, however, a very serious disadvantage and it is far outweighed by the sensitiveness of the method to small deviations from normal and by the consistency of its results which other methods lack.

To supplement the information given by the Spa Method in the more severe cases, I have for some time been using the Rourke and Ernstene (1929) method in parallel with it. This estimates the maximum velocity, during the period of steady fall, in mm. per minute. Correction for haematocrit reading is then applied by the use of Rourke and Ernstene's curve and the result is the Corrected Sedimentation Index (C.S.I.), the maximum velocity adjusted to haematocrit 45%. In practice a wide bore (5 mm.) Wintrobe tube was used and readings at ten-minute intervals enabled the maximum velocity to be estimated simultaneously on many tests. A correlation diagram is shown (fig. 3). It was found that among the most rapidly

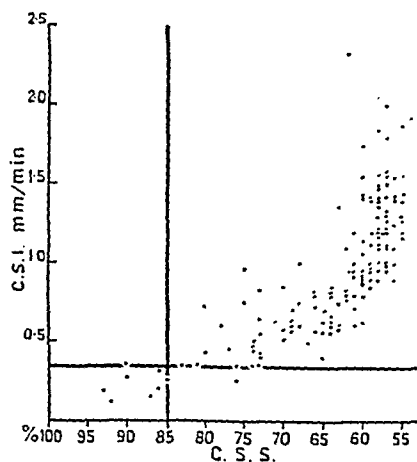


FIG. 3.

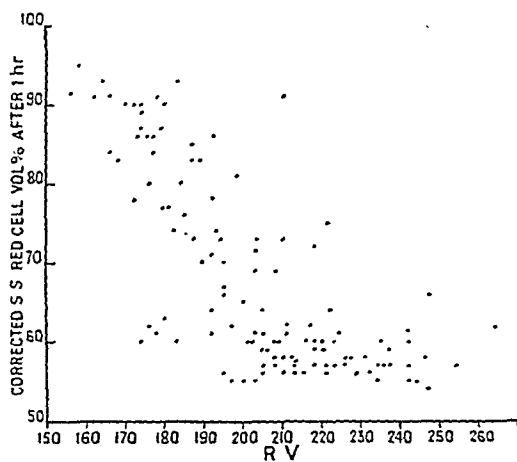


FIG. 4.

FIG. 3.—B.S.R. (corrected). Spa Hospital (C.S.S.) and Rourke and Ernstene (C.S.I.) in 142 observations on rheumatoid arthritis cases.

FIG. 4.—Relative viscosity (20°C.) and B.S.R. (C.S.S.). (Spa Hospital method.)

settling bloods the C.S.I. within one C.S.S. reading might vary from  $x$  to  $2x$ . For example 6 bloods of C.S.S. 58% had a maximum corrected velocity of 0.9 to 1.8 mm. per minute.

This is interesting and is being pursued further but it does not invalidate the conclusion that the B.S.R. as estimated by the Spa Hospitals Method affords a better differentiation between cases and controls than does the viscosity.

*Correlation of R.V. and C.S.S. in rheumatoid arthritis.*—Simple scatter diagrams (figs. 4 and 5) showed a wide distribution with a general correlation as previously shown by Woodmansey and Wilson (1948) using the same viscometer as we used and by Race (1948) using the Whittington viscometer. Fig. 5 shows a correlation study between the corrected sedimentation index and plasma relative viscosity. It is of interest because it gives evidence of the periodic relationship shown by Houston, Harkness and Whittington (1945). The peaks of the curve occur at R.V. 176, 187, 202, 213 and 233. Such a relationship is only seen when a corrected maximal velocity method is used for the assessment of the sedimentation rate. It will be recalled that the workers mentioned were dealing with cases of tuberculosis and they used different methods of estimating both sedimentation velocity and plasma viscosity. The agreement with their results is thus all the more significant as indicating that the relationship is a general one and not peculiar to one disease. It also suggests that the maximum velocity method of assessing B.S.R. reveals features which other methods fail to bring out. Tests showed that the correlation between viscosity and uncorrected B.S.R. was no better than that between viscosity and corrected rate.

The figures on which these graphs are based are shown in Table I. Relative viscosity is the basis of a narrow subdivision of the observations. In each group the cases are allocated to C.S.S. zones representing normal, doubtfully raised and rapid sedimentation rates. The range of the last is shown. It will be seen that there is a general tendency towards a correlation. The incidence of normal B.S.R. falls from 100% in the 150–159 viscosity group to zero in

TABLE I.—VISCOSITY AND B.S.R. (SPA HOSPITALS METHOD.)  
365 Observations on 286 Cases of R.A.

| R.V. 20° C. | B.S.R. (C.S.S.) |        |      |                      | Total | % Normal B.S.R. |
|-------------|-----------------|--------|------|----------------------|-------|-----------------|
|             | 85%+            | 80-84% | <79% | Range of C.S.S. <79% |       |                 |
| 150-59 ..   | 2               | 0      | 0    |                      | 2     | 100.0           |
| 160- ..     | 3               | 2      | 0    |                      | 5     | 67.0            |
| 170- ..     | 16              | 3      | 15   | 60-78                | 34    | 47.0            |
| 180- ..     | 9               | 6      | 51   | 59-79                | 66    | 14.0            |
| 190- ..     | 2               | 7      | 64   | 54-79                | 73    | 3.0             |
| 200- ..     | 1               | 1      | 74   | 54-73                | 76    | 1.3             |
| 210- ..     | 1               | 0      | 40   | 55-74                | 41    | 2.5             |
| 220- ..     | 0               | 0      | 44   | 55-75                | 44    | 0               |
| 230- ..     | 0               | 0      | 13   | 54-63                | 13    | 0               |
| 240- ..     | 0               | 0      | 9    | 54-66                | 9     | 0               |
| 250- ..     | 0               | 0      | 1    | 57                   | 1     | 0               |
| 260- ..     | 0               | 0      | 1    | 64                   | 1     | 0               |
| Total       | 34              | 19     | 312  |                      | 365   |                 |

viscosity groups 220 and higher. From the point of view of the clinician the most interesting point in the table is the viscosity range 170-179. Approximately half of these cases show a definite increase in B.S.R. and the range is a wide one including C.S.S. values as low as 60%. If to avoid this discrepancy the abnormal viscosity range were extended to include

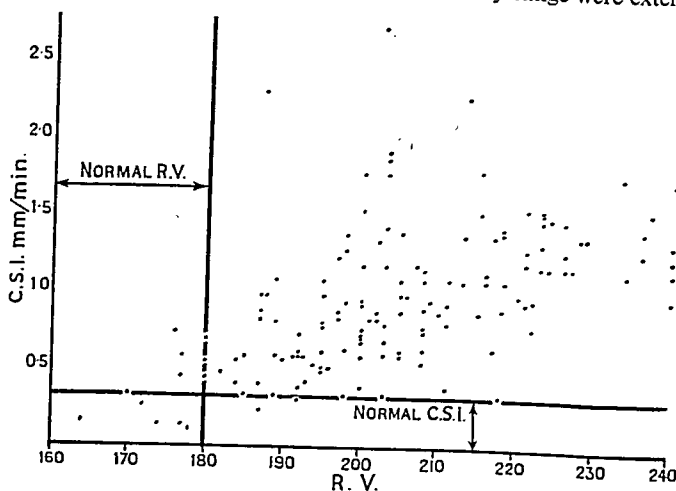


FIG. 5.—Relative viscosity and corrected sedimentation index (mm./min.).

the 170-179 group then it would include the highest single group of the normal controls. Of these 15 out of 41 had viscosity 170-179.

The conclusion seems to be justified that the B.S.R. as estimated by the Spa Hospitals Method is certainly not less sensitive to plasma abnormality than is the Relative Viscosity by the method used. Race (1948), employing the more accurate method of Whittington;

TABLE II.—VISCOSITY AND B.S.R. (SPA HOSPITALS METHOD.)  
365 Observations on 286 Cases of R.A.

| Viscosity       | B.S.R.                                            |          | Total | Percentage |
|-----------------|---------------------------------------------------|----------|-------|------------|
|                 | Normal                                            | Abnormal |       |            |
| Normal ..       | 21                                                | 20       | 41    | 11.2       |
| Abnormal ..     | 13                                                | 311      | 324   | 88.8       |
| Total           | 34                                                | 331      | 365   |            |
| Percentage ..   | 9.3                                               | 90.7     |       |            |
| B.S.R. only:    | Abnormality missed in 13 observations             |          |       |            |
| Viscosity only: | Abnormality missed in 20 observations             |          |       |            |
| Both tests:     | Abnormality demonstrated in 94.2% of observations |          |       |            |

found increased and even maximal sedimentation rates in presence of normal viscosity. The finding does not appear, therefore, to be peculiar to the Harrogate method of viscosity estimation.

*Further observation on discrepancies between relative viscosity and B.S.R. in R.A.*—All the patients examined were in some degree clinically active and it is of interest to find in what proportion the plasma tests failed to show evidence of this. From Table II it will be seen that the B.S.R. was normal in 34 cases (9.3%) and the viscosity was normal in 41 cases (11.2%). If the B.S.R. alone had been taken the abnormality of plasma shown by the increased viscosity would have been missed in 13 cases. Similarly the viscosity alone would have missed activity in 20 cases shown to be abnormal by the B.S.R.

If both tests were carried out the very high figure of 344 (94.2%) of a series of tests on rheumatoid patients could be shown to be abnormal. The 21 observations normal in both B.S.R. and Relative Viscosity included a small number of cases which were clinically very active, with wasting of muscle, anaemia and pain. They were quite typical of R.A. It must be recognized, as is the experience of all who have handled R.A., that a small proportion of cases fail to react by the production of the plasma protein changes responsible for the abnormal results in these tests. This failure of reaction may correspond with the "terminal decay" found in tuberculosis subjects by Harkness *et al.* (1946).

By carrying out *both tests* a very high degree of sensitiveness is achieved.

*Repeated tests on the same patient.*—78 examples of repeated tests at intervals of a week or more were available.

A difference of 3% C.S.S. and 5 in the relative viscosity ( $\times 100$ ) was taken as significant of difference. Of the 78 pairs of observations 47 showed agreement in the trend of B.S.R. and viscosity and 31 showed disagreement.

The disagreement in some cases was very great and both tests in certain cases disagreed with the short-term assessments of the patients' clinical condition. Cases could be quoted in which the B.S.R. agreed better with the clinical state and an equally good case could be made out for the viscosity as showing better agreement. Thus one case following transfusion showed remarkable clinical improvement amounting almost to remission. The B.S.R. became normal but the viscosity remained high. In a short time relapse occurred and the B.S.R. again became rapid. While the S.R. in such a case is more strictly correlated with the superficial evidences of improvement the viscosity was a more reliable index of the underlying process.

The conclusion seems to be warranted that B.S.R. and viscosity are measuring two different aspects of plasma abnormality. The B.S.R. is mainly influenced by fibrinogen, the viscosity by the total protein picture with globulins predominant. I cannot agree with the statement that because the tests do not agree then one of them must be inaccurate. Both may be perfectly accurate indices of different facets of abnormality in the same plasma.

*The time factor as a cause of discrepancy between B.S.R. and R.V.*—In searching for some cause for the discrepancy noted it was observed that certain cases of acute non-rheumatic disease showed a complete absence of correlation between the B.S.R. and viscosity, the former being very rapid and the latter normal. They included acute septic and virus diseases such as acute atypical pneumonia. In one such case the C.S.S. was 62% with viscosity 157.1. In another 62% with viscosity 174.3.

A patient seen at the onset of subacute infective endocarditis had C.S.S. of 74% with viscosity 163. A month later the C.S.S. was 60% and the viscosity had now risen to 186.1.

These results at once recalled the similar findings with the formol-gel test. In our first observations on this test (Gibson and Richardson, 1938) we noted an absence of correlation between B.S.R. and plasma-gel in acute gout. This was found later to be due to a time-lag in the development of the abnormal gel reaction as compared with the increase of B.S.R. Since the viscosity test has been used no cases of acute gout have been met. A consecutive series of 221 rheumatic cases was studied with simultaneous plasma-gel and viscosity estimations. The results are shown in fig. 6. Plasma-gel tests are positive in all cases in which the relative viscosity is over 210 and in the vast majority of those over 190. The incidence drops to 59% in the viscosity range just above normal (180–189) and is very low when viscosity is normal. This correlation is to be expected since both tests are concerned with the whole protein content of the plasma, especially the globulins.

It is of interest that Cowan and Harkness (1947) reported normal viscosity values in the early stages of rheumatoid arthritis.

*Viscosity and anaemia.*—Since both viscosity and anaemia are influenced by the clinical type of disease and its severity it is to be expected that a small degree of correlation be found.

This is seen in fig. 7, in which the percentage of cases with hæmatocrit under 40% in each viscosity group is shown.

The observation of Harkness *et al.* (1946) that a definite viscosity zone in tuberculosis was associated with pleural effusion raises the question of any inter-relationship between plasma viscosity and the distribution of intra- and extra-vascular tissue fluids. In rheumatoid arthritis an hydræmia has been frequently postulated to account for the very low packed red-cell volumes found in many cases.

The figures of viscosity and hæmatocrit readings were reviewed with this in mind. It was noted that if all observations showing hæmatocrit 35% or lower be taken, the viscosity in these cases was widely distributed throughout the whole range. It was found that 18% of viscosity readings in these low hæmatocrit cases were 230 or over while in the parallel series

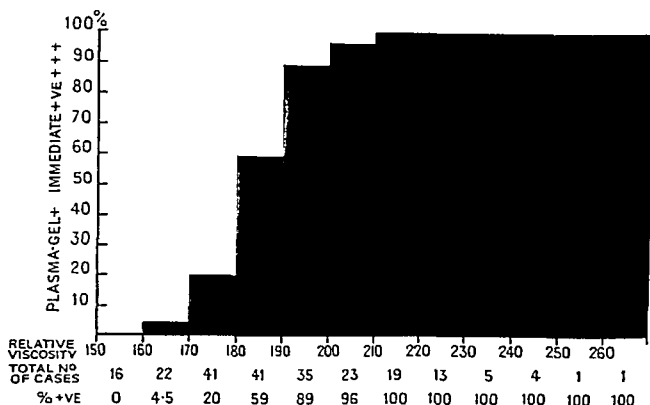


FIG. 6.—Plasma relative viscosity and plasma-gel in 221 consecutive cases.

with hæmatocrit 36% or more the proportion of viscosities over 230 was only 4.8%. There is therefore some association between anæmia or hydræmia and high viscosity as with the gel reaction (Gibson and Pitt, 1946) but it is not a direct one.

In connexion with anæmia it may be noted that in cases of primary anæmia and of anæmia due to hæmorrhage the viscosity value was normal and in full agreement with the corrected B.S.R. It did not agree with the rapid "crude" (uncorrected) rate noted in any of these cases. This gives support to the value of correction for anæmia in assessing the true B.S.R.

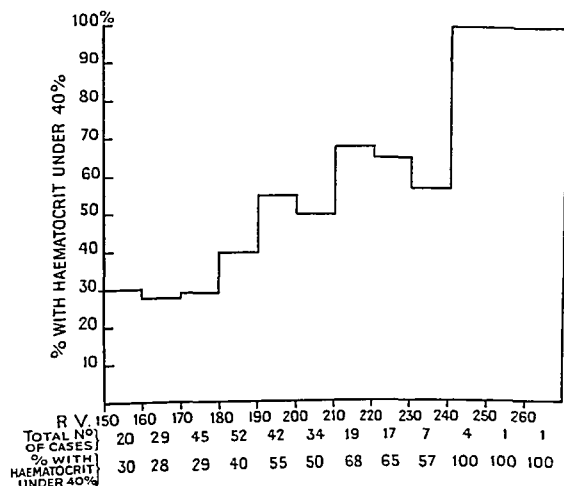


FIG. 7.—Plasma viscosity and hæmatocrit reading. Percentage of cases with hæmatocrit under 40% in each viscosity group.



*Viscosity and serum colloidal reactions.*—In 90 cases the relative viscosity was carried out in association with the serum colloidal gold, thymol turbidity and thymol flocculation tests. No correlation was found. This suggests that gamma globulin is not an important factor in influencing plasma viscosity.

*Viscosity in other clinical types of rheumatism.*—(1) *Ankylosing spondylitis.* The relative viscosity distribution in 34 cases of clinically active ankylosing spondylitis is shown in Table III. 3 cases show viscosity under 180. They were 176 (2 cases) and 178 so that in all

TABLE III.—ANKYLOSING SPONDYLITIS: RELATIVE VISCOSITY DISTRIBUTION IN 34 CASES

| Range of C.S.S. Reading is Given for Comparison |              |                       |
|-------------------------------------------------|--------------|-----------------------|
| R.V. ( $\times 100$ )                           | No. of cases | B.S.R. (C.S.S.) range |
| 150-159                                         | 0            |                       |
| 160-                                            | 0            |                       |
| 170-                                            | 3            | 60-82                 |
| 180-                                            | 4            | 66-82                 |
| 190-                                            | 5            | 61-81                 |
| 200-                                            | 8            | 53-93                 |
| 210-                                            | 7            | 58-76                 |
| 220-                                            | 3            | 56-63                 |
| 230-                                            | 4            | 55-63                 |

3 the results were "borderline". In all 3 the B.S.R. was increased, in 1 markedly so. In this series 1 case had a normal B.S.R. as shown by Spa Hospitals, Wintrobe and Rourke and Ernste methods. The relative viscosity in this case was 205.6.

All were clinically active. If both tests were considered all showed evidence of plasma abnormality. The viscosity alone would have failed to show this abnormality in 3 cases, the B.S.R. alone in 1 case.

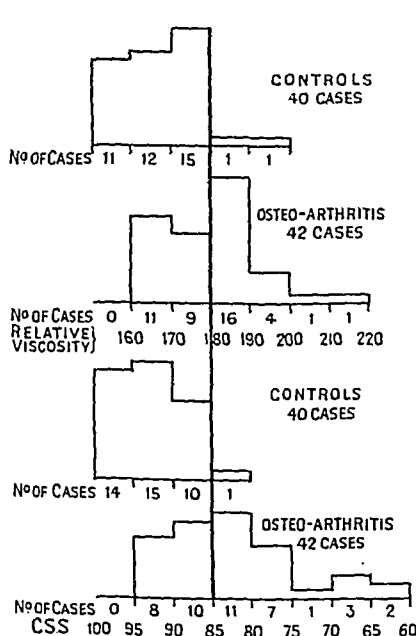


FIG. 8.—Osteo-arthritis.  
Viscosity and B.S.R.

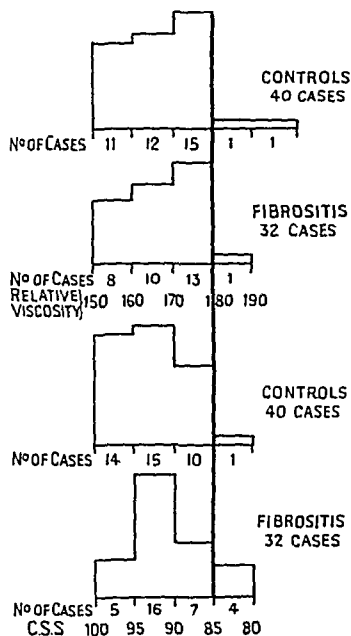


FIG. 9.—Fibrositis. Viscosity  
and B.S.R.

As in the R.A. group the conclusion seems to be warranted that the tests are estimates of different abnormalities which often but not invariably occur together. The B.S.R. is rather more sensitive but in order to secure the maximum of information both should be applied.

The raised relative viscosity in ankylosing spondylitis is of interest because in this condition the colloidal gold test is weak or negative in nearly all cases.

(2) *Osteo-arthritis*.—My experience has always been that in true osteo-arthritis, as found for example in the hip or knee, the B.S.R. is typically in a zone just outside the normal range. This is illustrated in fig. 8, in which the distribution of results in 42 cases is compared with 40 controls. The shift to the right is apparent.

The viscosity in the same series shows the same shift to the more abnormal groups. The highest number in the controls is in the 170–179 range while in osteo-arthritis it is from 180–189. As in the case of R.A. the graphs again show that the spread of B.S.R. results is further from the normal line than that of viscosity, indicating a rather greater sensitivity in the former.

The finding of an increased viscosity in osteo-arthritis as compared with normal is in agreement with Cowan and Harkness (1947).

(3) *Fibrositis*.—This entity is becoming less common in rheumatic disease hospitals partly because of priority given to the true arthritic and partly because, as a result of more accurate diagnosis, cases formerly diagnosed as fibrositis are now allocated to other groups, e.g. disc lesions. 32 cases were seen which satisfied the usual clinical requirements.

Fig. 9 illustrates the B.S.R. and viscosity findings. They are both quite normal. This agrees with the observations of Cowan and Harkness (1947).

#### COMMENT

The plasma viscosity is an important measure of plasma protein abnormality. The test is consistent in its results and abnormal readings are found in a large majority of cases of rheumatoid arthritis and ankylosing spondylitis. I agree with previous workers that it is not closely correlated with the B.S.R. At the same time the figures show that the inferences to be drawn from the two tests are largely in agreement. In fact the value of the test, in my opinion, lies in the fact that it views the plasma abnormality from a different angle and is therefore an independent or complementary assessment of activity. In the same way the colloidal gold and thymol turbidity tests show a further aspect of abnormality as it affects the gamma globulin. Their significance from the clinician's point of view appears to be less direct than that of B.S.R. and viscosity.

The lack of direct correlation between B.S.R. and viscosity was equally evident whichever method of assessing B.S.R. was used—crude, corrected and maximal. No association with anæmia was evident apart from the fact that both are influenced by the presence and activity of R.A.

*Relative value of B.S.R. and viscosity in management of cases*.—The difference in the spread of results between B.S.R. expressed by corrected suspension stability and viscosity has been noted and discussed. Briefly the deviation from normal in most cases is less in the case of viscosity. Again a study of active R.A., spondylitis and osteo-arthritis suggests that the B.S.R. is a more sensitive index of abnormality than viscosity in that a lower proportion of the former shows an abnormal reading in active cases, but certain active cases undoubtedly give plasma changes to which the viscosity test is more sensitive.

I have refrained from quoting individual cases. Any such selection may easily be misleading. The apparent unreliability of either test could have been shown by a suitable selection of cases. Clinical variations within the active state are almost impossible to estimate. The highest viscosity reading obtained was in a man who stated that he had been immensely improved following a course of intravenous therapy of a novel kind. His B.S.R. was maximal. Was he as well as he felt or as ill as his plasma tests suggested? In this connexion I wish to make a plea for agreement on a formula for the clinical assessment of activity in R.A. in simple terms capable of numerical expression. This has already been done in tuberculosis and suggested indices have been put forward for use in R.A. The patient's symptoms should have a part in such an estimate but objective evidence from physical signs should be heavily weighted, local and systemic effects being included.

The time relations of the plasma protein response to disease are interesting and may be of importance in diagnosis. It has been shown that in a group of acute non-rheumatic cases the B.S.R. was rapid in presence of a normal viscosity. In one such case a follow-up showed the development of increased viscosity at a later date. This recalls observations previously made that the B.S.R. increase precedes the development of the plasma-gel reaction. The plasma viscosity and gel reactions were found to be closely correlated, as indeed would be expected since both depend on the whole plasma protein picture and especially the total globulins. Such correlation is not, however, found in ankylosing spondylitis.

If a definite time relation could be established it would be of great value in general diagnostic work. It might prove possible, in a case showing a rapid B.S.R., to state that this is due to an acute or chronic process and some estimate of duration might even be possible.

## CONCLUSION

Viscosity estimation has an important place as an aid to the clinical assessment of activity in rheumatic disease. It supplements, but does not replace, the B.S.R. In any case or series in which a close watch is required on progress, both tests taken together give results which are more complete than either separately. The combination of tests should be of especial value in therapeutic trials in which for statistical purposes two independent indices would be available.

I am greatly indebted to Mr. E. W. Richardson for technical assistance in this work.

## REFERENCES

- COWAN, I. C., and HARKNESS, J. (1947) *Brit. med. J.* (ii), 686.  
 GIBSON, H. J., and PITT, R. M. (1946) *Ann. rheum. Dis.*, 5, 83.  
 ———, and RICHARDSON, E. W. (1938) *Acta. rheum. Amst.*, 10, 3.  
 HARKNESS, J., HOUSTON, J., and WHITTINGTON, R. B. (1946) *Brit. med. J.* (i), 268.  
 HOUSTON, J., HARKNESS, J., and WHITTINGTON, R. B. (1945) *Acta. tuberc. scand.*, 19, 153.  
 MACLAGAN, N. F. (1948) *Brit. med. J.* (ii), 892.  
 MILLER, A. K., and WHITTINGTON, R. B. (1942) *Lancet* (ii), 510.  
 RACE, J. (1948) *Ann. rheum. Dis.*, 7, 239.  
 ROURKE, M. D., and ERNSTENE, A. C. (1929) *J. clin. Invest.*, 8, 545.  
 WOODMANSEY, A., and WILSON, J. V. (1948) *Ann. rheum. Dis.*, 7, 235.

Dr. M. H. L. Desmarais: I would like to ask Dr. Gibson if the discrepancies he described between the corrected sedimentation stability and the plasma viscosity results may not be due to the presence of some other acute infection at that time? We all know that the sedimentation rate can be influenced by such acute conditions as the common cold, an attack of influenza, &c.

Bearing this in mind I would like to know if close clinical checks were made to exclude these conditions and also if the tests were repeated in such cases?

Dr. Gibson answered that all cases in which discrepancies between the sedimentation rate and the plasma viscosity tests were noted were reviewed clinically, and that many repeats of the tests were done, giving the same results.

Dr. Harry Coke: I wish to emphasize the importance of the simplicity of classification of arthritic conditions by histological technique. The recent tendency towards grouping a number of clinical syndromes under the one heading of "rheumatoid arthritis" has gained much support from this work.

Experience has been gained on the viscosity in some 400 cases of chronic rheumatic disease. It is important to have an instrument of the Whittington type calibrated to the original standard  $V_5$  instrument. Mr. Whittington has kindly calibrated my instrument, so that by experience, agreement to 0.002 can be guaranteed in an estimation in my laboratory with that of Dr. Harkness in his. The viscosity of serum is examined so as to avoid the additional electrolyte effect upon the colloidal equilibrium on which the physical factor of viscosity depends. In a chronic disease such as rheumatoid arthritis, these results prove entirely satisfactory. There seems no logical reason to assess the value of the viscosity by comparison with any other laboratory measurement, for it is a useful measurement on its own account. A statistical analysis shows a "correlation coefficient" between the Wintrobe E.S.R. and the serum viscosity of + 0.619, which is 6.6 times the standard error of the coefficient. The correlation coefficient of viscosity to the corrected E.S.R. is less significant than to the observed value. In clinical relationships the results agree very closely with those described by Dr. Gibson, except that in a group of inactive cases of spondylitis, every laboratory test was normal except the serum viscosity. My experience can be summarized by saying that the serum viscosity appears to be a useful addition to the assessment of the rheumatic patient, but that there is little evidence that it should or indeed will ever replace the erythrocyte sedimentation rate.

Dr. John Harkness (Portsmouth): Plasma [is a] colloidal solution and behaves as a non-Newtonian fluid, i.e. the "viscosity" value of any one plasma will differ from viscometer to viscometer because the "viscosity" is partly a function of the dimensions of the instrument (Harkness *et al.*). This difficulty has been overcome by calibrating viscometers with plasmas whose viscosities have been measured on an arbitrarily-chosen standard viscometer. The

majority of instruments in use in the medical laboratories of this country and in some foreign ones also are now calibrated in terms of one of my viscometers ( $V_5$ ) and as seen from our published results (Houston *et al.*) our values for similar clinical cases differ markedly from those produced by the viscometer as used by Dr. Gibson.

If we are to avoid a chaos similar to that arising from the multiplicity of E.S.R. techniques, we must adopt a single viscometry standard now, at the earliest stages in the use of the plasma viscosity test. At my request, the problem of such a single standard is being considered by the British Standards Institution. Until their findings are known, I will be glad to calibrate any new viscometer by plasma in terms of  $V_5$  and later prepare any necessary correlation formula to convert the values to the British Standards Institution scale.

#### REFERENCES

- HARKNESS, J. and WHITTINGTON, R. B. (1947) *Biochim. Biophys. Acta*, **1**, 487.  
HOUSTON, J., WHITTINGTON, R. B., COWAN, I. C., and HARKNESS, J. (1949) *J. Clin. Invest.*, **28**, 752.

**Dr. J. Euan Dawson:** My biochemical colleague and I have carried out about 250 estimations on rheumatoids.

These were done in a Woodmansey type tube and our results have been almost identical with those of Dr. Gibson. We have, however, used the wide tube method of E.S.R. and have had some quite extraordinary and unaccountable rises and falls in E.S.R. which have not shown a comparable rise or fall in the plasma viscosity (P.V.). In all these cases we have tried to correlate closely the P.V. with the clinical conditions. It has seemed that the P.V. is rather slower in its response, or more sluggish, and that perhaps it is not influenced so much by external factors such as colds or temperature as is the S.R.

I should like to ask Dr. Harkness whether it is really necessary for the P.V. estimation to be taken to two or more places of decimals; is the extreme accuracy essential from the clinical standpoint?

**Dr. John Harkness (in reply):** Measurement to the second place of decimals is essential, as changes in the figure in that position can be of significance in serial tests on individual patients.

## Section of Obstetrics and Gynæcology

President—Professor HILDA N. LLOYD, F.R.C.S., P.R.C.O.G.

[March 18, 1949]

### Obstetric Analgesia : A New Machine for the Self-Administration of Nitrous Oxide—Oxygen

By E. H. SEWARD, M.A., B.M., B.Ch.Oxon., D.A., D.Obst.R.C.O.G.

*Nuffield Department of Anaesthetics, University of Oxford*

This is a short report of experience in the Maternity Department of the Radcliffe Infirmary at Oxford with self-administered analgesia, using a fixed mixture of nitrous oxide—oxygen instead of the usual nitrous oxide—air mixture.

The apparatus used was designed by Andreas Warming of Copenhagen. The first model was made by the firm of Aga and called the Calmator. The present type has been in use in Denmark for several years, and has been on trial in the Nuffield Department of Obstetrics and Gynæcology in Oxford for more than a year. Nitrous oxide and oxygen are supplied from the usual cylinders with reducing valves: from there the gases pass to a mixing chamber, and thence to a reservoir bag from which the patient inhales through the usual wide-bore corrugated rubber tubing. The mixing chamber and reservoir bag are not cumbersome, the main bulk of the apparatus being due to the cylinders and the trolley which carries them.

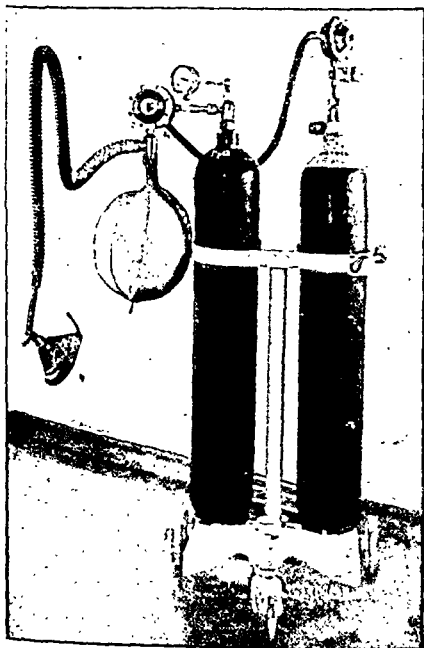


FIG. 1.—The whole apparatus assembled ready for use.

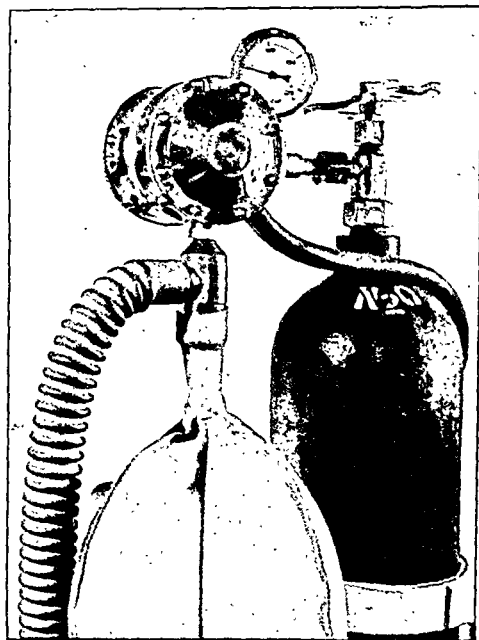


FIG. 2.—Close-up of the mixing-chamber and reservoir bag, which are the characteristic features of the apparatus.

An essential feature of the machine is the incorporation of a safety mechanism whereby, when the oxygen supply fails, the nitrous oxide is automatically cut off. In no circumstances, therefore, can the patient breathe pure nitrous oxide. The reservoir bag holds  $4\frac{1}{2}$  litres of gases ready for inhalation: as soon as some is inhaled, the bag is automatically replenished from the mixing chamber at the rate of 25 litres per minute. On laboratory analysis carried out in the Department of Anaesthetics, the gas mixture was found to be constant in com-

position irrespective of the rate and depth of respiration. A cylinder containing 100 gallons of nitrous oxide is enough for about four hours' continuous use and therefore about twelve hours' use in labour.

The apparatus as received was adjusted to give the mixture of 15% oxygen and 85% nitrous oxide used in Denmark. The first 60 cases were observed by Mr. J. B. Joyce, Obstetric House Surgeon. He found that 25, that is, almost half the total number, became partially anaesthetized: they were difficult to control and needed extra supervision. The machine was then adjusted to give 25% oxygen and 75% nitrous oxide. This mixture has been found satisfactory. It gives very effective analgesia, which usually develops within fifteen seconds or 6 breaths and can be maintained for five or more minutes during the actual delivery of the baby, without loss of consciousness, unless there has been very heavy premedication with analgesic and sedative drugs. The analgesia is more effective than that given by the usual 50% gas-air mixture, as shown by subjective and objective observation. Moreover, it can be maintained indefinitely without risk of anoxaemia. Patients appear to be more comfortable on the gas-oxygen mixture and it does not prevent their co-operation. In a planned test, 50 patients near the end of the first stage of labour, and having strong contractions, were given both gas-oxygen and gas-air and asked which was better. On account of the variable factors involved, 25 were given gas-oxygen first and later gas-air, while another 25 were given gas-air first and later gas-oxygen. The result clearly showed that gas-oxygen gave better pain relief.

The improvement is due to the higher proportion of nitrous oxide. At the same time gas-oxygen provides more oxygen than is possible with any gas-air mixture—25%, as opposed to 20% in atmospheric air or 10½% present in the usual gas-air analgesic mixture. Some patients become cyanosed when breathing the gas-air mixture: as is to be expected, this cyanosis disappears when they breathe the gas-oxygen mixture. This commends it for use in labour where there is cardiac disease, anaemia, or respiratory disease. From the baby's point of view it is probable that the extra oxygen is important. In 7 observed cases of foetal distress (bradycardia with heart-rate falling to 100 or less) when the mother used gas-air, the distress was relieved when the mother changed to gas-oxygen. This is in accordance with the views of Eastman (1936) that gas-oxygen mixtures containing 10% oxygen cause anoxaemia sufficient to lead to severe asphyxia of the baby.

Experience has shown that analgesia for self-administration in labour is more effective with this gas-oxygen mixture than with gas-air. The apparatus has proved satisfactory for routine use in a department dealing with normal and abnormal midwifery. It provides a high degree of pain relief and is of particular value where anoxaemia must be avoided. The new type of machine designed by Andreas Warming has given excellent service and for hospital purposes is preferable to other types of machine which make use of a gas-air mixture.

No special supervision has been found necessary when this apparatus is in use, and midwives trained in the use of gas-air employ it without difficulty. It has been used on and off in labours lasting several days, and also used continuously for long periods at a time without ill-effect; it is, however, clearly not desirable that in such long labours the patient should rely solely on self-administered analgesia. There appears to be no time limit for its use in any one labour: in prolonged labour it is especially valuable in that its effects are not cumulative and the avoidance of anoxaemia is of advantage to the baby.

*Acknowledgment.*—I acknowledge with thanks the permission to extend this trial to patients in the Area Department of Obstetrics and Gynaecology at Oxford.

#### REFERENCE

EASTMAN, N. J. (1936) *Amer. J. Obstet. Gynec.*, 31, 563.

The following cases and specimens were shown:

Spontaneous Double Rupture of the Uterus at 30 Weeks Pregnancy.—C. CHRISTOPHER BOWLEY, M.B., M.R.C.O.G.

Rupture of the Uterus in Labour as a Sequel to the Manchester Operation.—T. B. FITZGERALD, F.R.C.S.Ed.

Sarcoma of the Uterus.—G. L. DALY, M.B.

Traumatic Enlargement of the Clitoris.—JEAN BURTON-BROWN, F.R.C.S.

Dysgerminoma of Ovary.—MARGARET BOULTON, M.R.C.S., L.R.C.P., M.R.C.O.G.

Large Hamangioma of the Placenta.—IMMANUEL BIERER, M.D.

Carcinoma.—E. COPE, M.D., M.R.C.O.G.

[May 20, 1949]

## DISCUSSION ON THE TREATMENT OF CARCINOMA OF THE VULVA

Mr. Stanley Way: It is now ten years since the treatment of carcinoma of the vulva was discussed by this Society and in the intervening period there have been signs of a change of opinion in regard to both treatment and prognosis. There is an increasing awareness that radium and X-rays can do little to effect a cure in this disease. The vulva with its poor collateral circulation and the peculiar precancerous lesions which are so often encountered makes a poor situation in which to use radium, and the fearful necrosis which so often follows its application, even in reasonable doses, must be well known to all who have used it or seen it used in these cases. The fact that X-rays with our present equipment can do little to eradicate tumour from the lymph nodes is too well known to require any elaboration here.

It would appear then that surgery is the method of choice in the treatment of cancer of the vulva, and indeed, there is no other situation in the body in which carcinoma appears, the breast included, which is more suitable for a radical surgical attack. Free as its lymphatic drainage is, it is perfectly accessible surgically in its first, second and third relays and if necessary in its fourth and fifth. Ideally the perfect operation for cancer must include the wide removal of the primary, and any pre-malignant lesion from which fresh primaries might develop, and at least the first and second group of lymph nodes and more, if possible. All this can be done in the case of carcinoma of the vulva.

In discussing the surgical treatment of vulval cancer I am going to confine myself to the extended radical operation that I have practised continuously for the last six years. The operation consists of the very wide removal of the vulva, the resection of the superficial inguinal and subinguinal lymph nodes, the incision and medial displacement of the external and internal oblique and transversalis muscles and the peritoneum, the division of the inguinal ligament and the routine removal of the lymph node of Cloquet, and the external iliac lymph nodes as high as the bifurcation of the common iliac vessels—and higher if the findings at operation seem to warrant it. I devised this after studying the many cases which I was able to follow up in Newcastle and from a study of the records of past cases; in all there were about 250 cases and records upon which to work.

In the first place the results of surgical procedures which had been previously employed were not encouraging. Of 87 cases treated in Newcastle by means of simple vulvectomy or local excision of the tumour, a quarter survived five years and the only remarkable fact is that so many survived such an illogical operation. Only 9.7% of patients treated by diathermy coagulation survived five years, but too great attention should not be paid to this very poor figure, since the method introduced by Berven (1941) and his associates was never properly carried out in this series, and Berven's own figure of nearly 40% five-year survivals probably represents the best that can be achieved with this method. The next method is that of hemivulvectomy with the dissection of the superficial nodes on the same side as the tumour. The results in the small series that I was able to find in Newcastle were very poor and we have abandoned this operation long ago. I personally have never done it or seen it done, but I have seen some cases upon which it had been performed. As I shall presently show it is based on a complete lack of understanding of the lymphatic anatomy of the vulva, and it transgresses every one of the principles of a radical operation for cancer.

Finally there was removal of the vulva with bilateral superficial node dissection. All the node-involved cases died before five years and the five-year survival rate was 21%.

I followed up these cases and finally performed autopsies on many of them. I found there were recurrences locally in the region of the removed vulva in cases where the primary tumour was anything but very small; and there were secondary deposits in the iliac lymph nodes in cases where the inguinal nodes were involved. These were the two main causes of failure but in addition there were a number of second primaries in residual areas of leukoplakia in those that lived long enough to get them, and also a small number of recurrences in the groin scars when the nodes had been involved. These were the problems that had to be solved.

The prevention of recurrences and the development of fresh primaries called for a much wider removal of the vulva than had hitherto been carried out, and so I introduced the wide *en bloc* removal, leaving the wound open and exposing the periosteum of the symphysis and the external obturator muscles (see fig. 1). There is no possibility of closing the wound and if there is, then the operation has not been properly performed. This wide removal may have to include a large amount of urethra or the removal of the anus with the establishment of a permanent colostomy. I have done this several times with no ill-effects and these obstacles of urethra and anus are more apparent than real.

The next problem was the question of the lymph nodes. Most workers have found in-

volved nodes in about 50% of cases. In the 88 cases that I had for close study whilst working out this technique I found the incidence to be 51% although in the 64 extended radical operations that I have performed it is only 36%. The most important question was the mode of spread of the tumour in the lymphatics. The lymphatics of the lower two-thirds of the vulva and most of those from the upper third go first to the superficial inguinal nodes, but what is very important is the fact that *they may go to the opposite groin*. In the 45 node-involved cases which I studied whilst working on the anatomy of this subject I found contralateral and bilateral node involvement in 18 cases altogether. If one excludes tumours that were crossing the mid-line there were 12 cases of bilateral or contralateral node involvement in 30 cases of unilateral tumours with involved nodes or 40%. The figure for bilateral involvement of nodes in mid-line tumours showing node involvement is very high. In my small series it was 86%. So much for the rationale of dissecting the nodes only on the side in which the tumour is situated.

To refer once more to the anatomical pathway, the next relay from the superficial inguinal nodes is to the deep femoral node. There are said by the anatomists to be three of these. I have never found more than one, but this is the all-important lymph node of Cloquet lying high in the femoral canal and projecting into the pelvic cavity. There are three points about this node : (1) Almost all the lymphatic drainage of the vulva passes through it. (2) It receives directly lymph trunks from the clitoris and upper part of the labia, and (3) In most cases it cannot be satisfactorily exposed without dividing the inguinal ligament.

From this node the lymphatics pass to the external iliac nodes and from there to the common iliac group and so to the para-aortic nodes. This arrangement is shown diagrammatically in fig. 2. It seemed therefore that by an extraperitoneal exposure all these nodes could be removed, and in 1941 I tried the operation on a patient who had involved nodes and who died from heart failure at the age of 75, at the beginning of May 1949, eight years after operation, with no recurrence of the carcinoma. This woman had a stormy time and was five months in hospital and it was indicated to me at that time that this sort of thing was not very popular. I therefore went on collecting information mostly of a negative type, showing the futility of minor surgery in this disease. There were, however, two points to which I directed my attention. The first of these was the unreliability of palpation as a method of determining whether or not the lymph nodes were involved. Of 27 cases with enlarged nodes only 55% were involved, but, and this is more important, in 36 cases in which the nodes were not enlarged 39% were found microscopically to contain cancer. Thus diagnosis by palpation appears liable to a 42% error. At autopsy I found recurrences in the groin scars to be of two types : (a) those in which a node or two had been left behind in the original groin dissection, and (b) where no nodes had been left but where there were recurrences in the scar or subcutaneous tissues. Clearly in the second type a node containing cancer must have been incised during the original operation and tumour cells implanted in the surrounding tissues. This is the chief reason why I introduced the removal of the skin flap from the groin. The upper incision is placed above the line of the nodes and the lower below it, and it is surprisingly easy to remove the nodes without danger once this flap has been fashioned. In addition it lessens the risk of undercutting the edges and improves wound healing. I do not have so many broken-down groin wounds as I had before I started using it, nevertheless even now at least half of my groin wounds do not heal by first intention.

Having worked out these details and performed the operation once, I looked around for further support for my theories as I did not imagine that this technique was original. I eventually found confirmation in the work of Stoeckel (1930) in Germany who had performed a similar operation with success, and mostly in the work of Taussig (1941) who followed Basset's suggested approach, but neither of these surgeons employed the free removal of the vulva with their wide lymphatic dissection. Taussig did his cases in two stages, removing the nodes first and the vulva later, but I have done most of my operations in one stage.

Now it might be expected that even though the results of this operation are good, the operative mortality will be high and the operability low. I will review my results to date.

I have attempted the operation on 64 occasions and completed it in 62. When estimating operability I must exclude two cases, that is—Case 1, which was the experimental operation performed in 1941, and the case which I have called 64 in this series. I operated on this patient earlier this year at the Samaritan Hospital. It was selected for me for demonstration purposes and was an extremely favourable case for treatment. This means that out of 62 cases upon whom I thought I could operate I succeeded in 60 cases, and during those years I rejected 9 others on account of too advanced disease (3 cases), concomitant disease (4), concomitant disease and advanced age (1) and advanced age and debility (1); thus out of a total of 71 cases seen between 1943 and May 1949 I have operated and completed the operation in 60 and therefore my operability rate is 85%. I have taken every case sent to



the Newcastle centre, and far from having them picked because they were good cases for operation, I know that one or two of the neighbouring centres have preferred to do local operations on the early cases and refer to me the large, advanced and difficult ones. If I were to start this series again I think I could have completed the 2 cases which I failed to finish and would include 5 out of the 9 that I rejected.

The next matter to consider is the operative mortality, although since these patients have very little hope without surgery this is perhaps not so important. To those who think that at all costs the patient must leave hospital alive I would advise a close attendance at the follow-up clinic and regular visits to the wards of a chronic hospital where the fruits of their conservatism—for only by conservatism can the operative mortality be kept very low—will stare

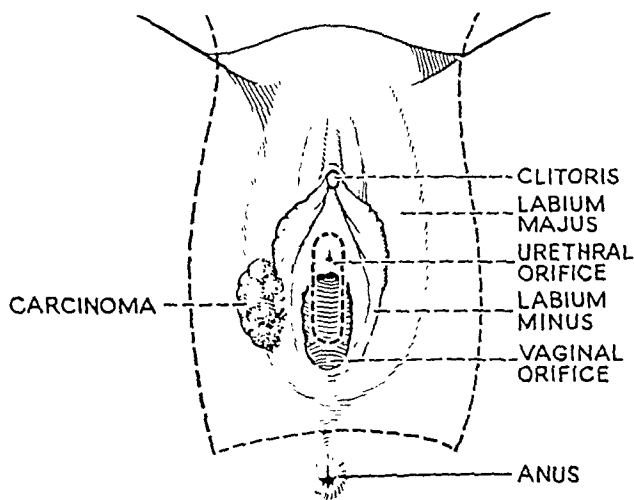


FIG. 1.

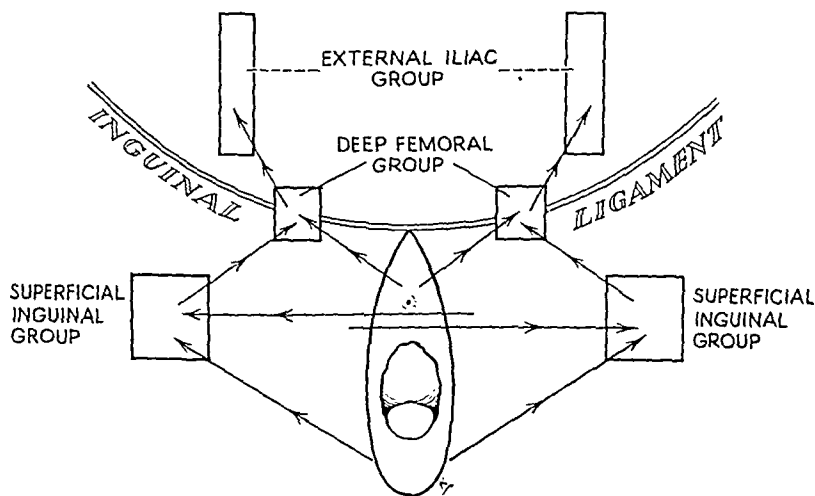


FIG. 2.

them in the face. I would remind them of the words of the late Charles Mayo who, when he had sat patiently through a meeting at which various surgeons had given descriptions of their operative mortalities ranging from 1 to 4% for resections of the stomach for cancer, gave it as his opinion that "anyone who didn't have a mortality of 10% wasn't even trying to cure cancer."

In assessing my operative mortality I am going to include all the 64 operations, and all the deaths in patients before their discharge from hospital. There were 10 of these, including 1 of the 2 incomplete operations and 1 from cerebral hæmorrhage three months after opera-

tion in a patient who was too ill from concomitant disease to be discharged. This gives an operative mortality of 16%.

The chief cause of death has been wound infection, no less than half the fatal cases being due to this, which also contributed to some of the others. The wounds readily became infected with all manner of organisms, many of which, like *B. proteus* and *B. pyocyaneus*, do not show any sensitivity to penicillin or sulphonamides and can cause untold havoc in a wound. I hope that streptomycin will help in this connexion, but it is not a drug that can be used indiscriminately as many use penicillin at present. Extreme care in nursing these cases will do more than any number of antibiotics and when we find the solution of the problem of wound infection the mortality of this operation will drop to below 10%.

I can only give a small number of five-year results as only 12 of these cases were operated on more than five years ago, and 1 of these, namely the 1941 case, perhaps ought to be excluded for the sake of statistical accuracy. This leaves 11 cases, 4 of which had involved lymph nodes. One died of the operation and during this time I rejected one case so that the absolute five-year survival rate is 83%. Small as the series is, I think this figure must at least arouse some interest. My three-year survival rate for a series of 27 cases is 86%.

TABLE I

| No. | Age | Remarks                             | Result                                                              | No. | Age | Remarks                                                    | Result                             |
|-----|-----|-------------------------------------|---------------------------------------------------------------------|-----|-----|------------------------------------------------------------|------------------------------------|
| 1   | 67  | Involved nodes                      | Died 8 years; heart disease; No rec.                                | 17  | 29  | Recurrent tumour                                           | Alive and well 4 years             |
| 2   | 59  | Involved nodes                      | Died 5½ years; Carcinoma of larynx; No rec.                         | 18  | 67  |                                                            | Alive and well 4 years             |
| 3   | 50  | Two-stage opn.                      | Alive and well 5½ years                                             | 19  | 46  | Involved nodes                                             | Alive and well 4 years             |
| 4   | 42  |                                     | Alive and well 5½ years                                             | 20  | 62  | Involved nodes                                             | Alive and well 4 years             |
| 5   | 45  |                                     | Alive and well 5½ years                                             | 21  | 52  | Pernicious anæmia                                          | Alive and well 3½ years            |
| 6   | 34  | Involved nodes deep and superficial | Alive and well 5½ years                                             | 22  | 50  | Involved nodes                                             | Alive and well 3½ years            |
| 7   | 46  |                                     | Alive and well 6 years                                              | 23  | 72  | Subsequent carc. anus and rodent ulcer of nose             | Alive and well 3½ years            |
| 8   | 70  | Involved nodes                      | Alive and well 6 years                                              | 24  | 60  | Involved nodes, superficial and deep; operation incomplete | Died 2 months. Pelvic metastases   |
| 9   | 68  |                                     | Alive and well 5½ years                                             | 25  | 64  | Tumour 5 in. square                                        | Died. Septic pneumonia 10 days     |
| 10  | 63  |                                     | Post-operative death. Respiratory failure due to general anæsthesia | 26  | 66  | Heart disease                                              | Died. Post-operative heart failure |
| 11  | 56  | Involved nodes                      | Alive and well 5 years                                              | 27  | 58  | Involved nodes, superficial and deep                       | Died 8 months. Remote metastases   |
| 12  | 64  |                                     | Alive and well 5 years                                              |     |     |                                                            |                                    |
| 13  | 67  |                                     | Alive and well 4½ years                                             |     |     |                                                            |                                    |
| 14  | 28  | Subsequent pregnancy                | Alive and well 4½ years                                             |     |     |                                                            |                                    |
| 15  | 56  |                                     | Alive and well 4½ years                                             |     |     |                                                            |                                    |
| 16  | 65  |                                     | Alive and well 4½ years                                             |     |     |                                                            |                                    |

I am still in favour of the one-stage operation if it can be done safely, but in cases of advanced age or concomitant disease it can be carried out in two or three stages. Where the growth extends well into the inner side of the thigh and there is a mass of nodes in the groin then I would advise removing the vulva and dissecting that groin at one stage. If I had done this I might have lessened the risk of groin recurrence in the only case in this series where it has occurred. Here, however, I had the dice loaded against me. This woman presented with a mass of nodes in the groin the size of a foetal head. Her doctor had been aspirating this for a month and, failing to get pus, he referred her to hospital for incision of abscess, where of course the small vulval primary was discovered. An implant appeared in the thigh, well away from my incision, three months after operation and although I excised all the structures of the inner aspect of the thigh, including the adductor muscles, fresh implants began to develop all over the area. I feel that this tumour was well and truly implanted before we ever saw it.

The wide removal of the vulva is, I am sure, the most important step in the operation, and the necessity of widely removing the lymphatics is not far behind in importance, although exactly what the operation can do in this way cannot be obvious at this stage. In Taussig's series there was surprisingly little difference in his node-involved results and those that he obtained when the nodes were not involved, and that is borne out by my five-year figures as far as they go. I would not like to minimize the difficulty of this operation for it is never simple and is often quite difficult. There is a good deal to be done and if it is to be carried out thoroughly in one stage it demands a surgeon who is a quick operator. The longest time that I have taken on a one-stage operation, my first, was three hours; the shortest was on a very thin old woman on whom I completed the operation in one hour and

ten minutes. I purposely tried to hurry this case as the patient was 72 and very frail, but I found it most tiring.

Far more complicated and exacting than the operation is the after-care of these patients. Time and again I have seen my results almost brought to nought by inefficient nursing, and often when the nursing was efficient the facilities to use that efficiency to the full were not available. Many of these cases I did in an emergency centre where cross-infection was rife, but I was very gratified to see the excellent progress made by the patient that I operated on at the Samaritan Hospital early this year and also by those I have treated in my new unit in Newcastle.

Now carcinoma of the vulva is not a very common disease. The figures from the Registrar-General show that about 400 women die in a year of this form of cancer in England and Wales. This is almost certainly an underestimate since practitioners are notoriously inaccurate in signing death certificates. Between 1910 and 1943 there were 47 untreatable cases of carcinoma of the vulva seen in the Infirmary at Newcastle. All were confirmed and all died within a year of discharge. I got copies of their death certificates and 15 were said to have died from carcinoma of the vulva. The other 32 were mostly registered as carcinoma of the uterus, but some were signed up as syphilis and one as senility. Let us say then that there may be 600 cases occurring annually in England and Wales; even this is not a large figure when they are distributed throughout the country as a whole. In 1939 when the subject was last discussed by this Society, Professor F. J. Browne (Browne, 1939) suggested that since the disease was not common the cases should be pooled and sent to selected clinics so that some people at least could get a good deal of experience. As a result of this I was able to persuade my colleagues in Newcastle to let me have all the cases they saw, and by their unselfish attitude I have seen 127 cases of carcinoma of the vulva in the last ten years. This is approximately 13 times as many as the average gynaecologist sees in the same time. I have recently written to a number of centres in Great Britain in an attempt to ascertain how frequently carcinoma of the vulva is seen and I am very grateful to all who sent me information on this subject. Table II shows the figures for some London Hospitals. In seven teaching hospitals in six years, 21 surgeons saw an average of one case a year.

TABLE II.—LONDON. 1936-8 AND 1946-8  
Gynaecologists Cases

| Teaching hospitals                 |          |           |
|------------------------------------|----------|-----------|
| *A                                 | 3        | 48        |
| B                                  | 3        | 9         |
| C                                  | 3        | 16        |
| D                                  | 3        | 8         |
| E                                  | 3        | 19        |
| F                                  | 3        | 18        |
| G                                  | 3        | 8         |
| Non-teaching Hospitals             |          |           |
| A                                  | 2        | 0         |
| B                                  | 4        | 20        |
| Special Hospitals (Gynaecological) |          |           |
| A                                  | 10       | 30        |
| Special hospitals (Cancer)         |          |           |
| A                                  | 7        | 64        |
| B                                  | 1        | 36        |
|                                    | <hr/> 45 | <hr/> 276 |

Average—1 case per surgeon per year.

TABLE III.—PROVINCES (INCLUDING WALES, SCOTLAND AND IRELAND). 1936-8 AND 1946-8  
Gynaecologists Cases

| Teaching hospitals                 |          |           |
|------------------------------------|----------|-----------|
| A                                  | 5        | 48        |
| B                                  | 4        | 77        |
| C                                  | 4        | 60        |
| D                                  | 2        | 6         |
| E                                  | 3        | 16        |
| F                                  | 4        | 20        |
| G                                  | 6        | 40        |
| Non-teaching hospitals             |          |           |
| A                                  | 1        | 1         |
| B                                  | 1        | 51        |
| C                                  | 1        | 4         |
| D                                  | 2        | 13        |
| E                                  | 1        | 6         |
| F                                  | 1        | 14        |
| G                                  | 1        | 8         |
| H                                  | 1        | 4         |
| I                                  | 3        | 24        |
| J                                  | 2        | 62        |
| K                                  | 2        | 18        |
| L                                  | 2        | 26        |
| M                                  | 2        | 20        |
| N                                  | 1        | 14        |
| O                                  | 1        | 12        |
| P                                  | 1        | 7         |
| Special hospitals (Gynaecological) |          |           |
| A                                  | 3        | 11        |
| B                                  | 5        | 34        |
|                                    | <hr/> 59 | <hr/> 596 |

Average—1.7 cases per surgeon per year.

\*This hospital has a long-established and well-known cancer clinic.

In the provinces the position is very little better. Table III shows the average there to be 1.7 cases per surgeon per annum and varying from an average of nearly eight a year in one centre to one case in six years in another. These provincial figures do not include Newcastle.

In this disease I am certain that in the best circumstances there should be over 60% five-year cures. There is one further reason for concentrating these cases; so frequently in carcinoma of the vulva one sees the pre-malignant and the malignant lesion side by side; here is valuable material for research. In Newcastle in spite of lack of space and money we have made a small start on the problem.

If the cases are sorted out and referred to a centre for treatment of carcinoma of the vulva, we shall get good results and more cases could be treated surgically.

I am indebted to Sir Cecil P. G. Wakeley, P.R.C.S., Editor of the *Annals of the Royal College of Surgeons, England*, for permission to reproduce figs. 1 and 2.

#### REFERENCES

- BERVEN, E. (1941) *Acta radiol. Stockh.*, 22, 100.  
 BROWNE, F. J. (1939) *Proc. Roy. Soc. Med.*, 32, 308.  
 MAYO, C. W. Quoted by Finch, E. F. (1948) Personal communication.  
 STOECKEL, W. (1930) *Zbl. Gynäk.*, 54, 47.  
 TAUSSIG, F. J. (1941) *Amer. J. Roentgenol.*, 45, 813.

Mr. J. B. Blaikley: With the kind permission of my colleagues I have tried to analyse the results of treatment of carcinoma of the vulva at the Chelsea Hospital for Women and the Royal Cancer Hospital, for the years 1933 to 1943 inclusive. Owing to deficiencies in the follow-up a complete analysis was impossible, so I have confined myself to one or two aspects of treatment.

#### Results at Chelsea Hospital for Women :

|                                                 |    |    |    |     |
|-------------------------------------------------|----|----|----|-----|
| Total number of patients                        | .. | .. | .. | 29  |
| Five-year survival                              | .. | .. | .. | 11  |
| Five-year survival rate (relative)              | .. | .. | .. | 38% |
| The absolute survival rate cannot be calculated |    |    |    |     |

There were 14 earlier cases, with ulcers no bigger than 4 cm. diameter, and with no clinical evidence of involvement of the inguinal glands. Of these 10 were treated by excision or simple vulvectomy, 5 died (4 within two years) and one patient is untraced. All died of recurrent carcinoma. The survival rate after five years is only 40% among this group.

The remaining 4 early cases were treated by vulvectomy and inguinal lymphadenectomy (3 cases), deep X-rays to the glands (1 case). All 4 were alive at the end of five years.

#### The results at the Royal Cancer Hospital are similar:

|                                    |    |    |    |     |
|------------------------------------|----|----|----|-----|
| Total number of patients           | .. | .. | .. | 49  |
| Five-year survival                 | .. | .. | .. | 23  |
| Five-year survival rate (relative) | .. | .. | .. | 47% |
| (9 cases were untraced)            |    |    |    |     |

There were 16 cases with ulcers not bigger than 4 cm., and no clinical evidence of glands being involved. Of these, 8 were treated by simple excision of the vulva or some part of it: 4 were alive after five years and 4 had died, all 4 within two years; all died of recurrent carcinoma. The survival rate after five years is 50% of this group.

Of the remaining 8 cases, 2 were treated with radium only, neither can be traced. Of the other 6 cases, in 2 the inguinal glands were excised, in 2 telerradium was applied to the groins, and in 2 deep X-rays were given to the groins. All 6 were alive after five years.

If any further evidence were needed to condemn simple excision or vulvectomy, here it is. There is very little improvement in the five-year survival rate for these earlier cases on that for the total number of cases (all stages), whereas it ought to be considerable. The remaining patients have been treated in such a variety of ways that it is not possible to give useful figures.

Because only a few cases of carcinoma of the vulva are seen by any one gynaecologist each year, inadequate surgery is all too common. The choice of treatment lies between radical surgery or, if the patient is unfit, after excision of the vulva, telerradium may be applied to the groins. In actual fact few elderly women, with modern anaesthesia, are unfit for surgery. My experience is nothing like as great as Mr. Way's, but of recent years I have seen quite a few cases of carcinoma of the vulva. I do not consider that in the majority of cases it is necessary to remove the iliac glands, but it is necessary to make a complete

removal of the superficial inguinal glands and of the deep femoral group. I have been able, I believe, to remove the gland of Cloquet from the femoral canal from below. The iliac glands are only involved very late, and the extended Basset's operation is I think unnecessary, therefore, except in advanced cases, but all too often these cases are inoperable owing to fixation and necrosis of the inguinal glands.

In November 1947 Professor Berven of the Radiumhemmet, Stockholm, read a paper in this country before the Faculty of Radiologists, which appears in the *British Journal of Radiology* (1949) 22, 498. Professor Berven treats carcinoma of the vulva by electro-coagulation of the vulva and telerradium to the groins, followed by lymphadenectomy in selected cases.

He coagulates the whole of the vulva using a 1 to 2 amp. current at 100 volts, wave-length 500 m. A temperature of 80–90° C. is produced locally, 40–50° C. at the inguinal fold. At the end of a week sloughing commences and lasts two weeks. Healing is surprisingly rapid and a supple scar results. If the glands do not disappear or, in spite of telerradium, lymphatic metastases appear later, Professor Berven excises the inguinal glands. There is very little shock from this treatment and surprisingly little pain, even where the most extensive coagulation is performed. At the end of a week it is possible for the patient to get out of bed and move about and to get into a bath. It is possible for her to go home before healing is complete.

Berven gives the following figures:

|                                    |    |       |
|------------------------------------|----|-------|
| Total number of patients seen      | .. | 384   |
| Total number of patients treated   | .. | 286   |
| Five-year survival (symptom free)  | .. | 109   |
| Five-year survival rate (relative) | .. | 38.1% |
| Five-year survival rate (absolute) | .. | 26%   |

He says 241 patients were clinically operable, and the five-year survival rate for this group is 43.2%.

The detailed figures he gives allow me to calculate his results for those cases without involvement of glands on examination, and in which the growth was not extensively involving tissues other than the vulva. There are 111 cases giving 67 five-year survivals, i.e. 60%. This is a group comparable with the two similar small groups from Chelsea Hospital for Women, and the Royal Cancer Hospital.

For a comparable group of cases *qua* local extent of the growth, but with glands evident clinically but operable, there were 83 cases, and the five-year survival rate is 31.3%. These figures of Berven's are good, and since it is a big series of cases they make a good yardstick by which to judge results of other treatments.

Taussig's figures for the complete Basset's operation are a little better, but his series of 41 cases is small. In his paper (*Amer. J. Obstet. Gynec.*, 1940, 40, 764) he gave the following figures:

|                             | Cases | Five-year survival | %    |
|-----------------------------|-------|--------------------|------|
|                             | 41    | 24                 | 58.5 |
| Glands show growth .. ..    | 19    | 10                 | 52.6 |
| Glands show no growth .. .. | 22    | 14                 | 63.6 |

There were 45 operations under 65 years with 1 death, and 23 operations over 65 years with 4 deaths.

#### CONCLUSIONS

(1) The whole of the vulva must be excised, preferably with the diathermy knife, or else destroyed by electro-coagulation.

(2) The inguinal glands must always be treated: if there is clinical evidence of metastases, a block dissection of the superficial inguinal and deep femoral groups should be done; if there is no clinical evidence of involvement, I am uncertain of the best course—in a patient who is a good surgical risk I would favour lymphadenectomy, but in others I would favour telerradium, but it may be that the latter is the better course in all such cases, and the glands should be excised only if later there is evidence of metastasis, as Berven has done.

(3) I would advocate electro-coagulation of the primary growth where it is locally extensive and because of this and also, maybe, the patient's age, surgery is not applicable.

(4) Metastasis in the iliac glands occurs late, and the removal of these glands is only occasionally necessary. In advanced cases all too often the inguinal glands are already fixed and inoperable, but, if not, the complete Basset's operation should be done.

In the provinces the position is very little better. Table III shows the average there to be 1.7 cases per surgeon per annum and varying from an average of nearly eight a year in one centre to one case in six years in another. These provincial figures do not include Newcastle.

In this disease I am certain that in the best circumstances there should be over 60% five-year cures. There is one further reason for concentrating these cases; so frequently in carcinoma of the vulva one sees the pre-malignant and the malignant lesion side by side; here is valuable material for research. In Newcastle in spite of lack of space and money we have made a small start on the problem.

If the cases are sorted out and referred to a centre for treatment of carcinoma of the vulva, we shall get good results and more cases could be treated surgically.

I am indebted to Sir Cecil P. G. Wakeley, P.R.C.S., Editor of the *Annals of the Royal College of Surgeons, England*, for permission to reproduce figs. 1 and 2.

#### REFERENCES

- BERVEN, E. (1941) *Acta radiol. Stockh.*, 22, 100.  
 BROWNE, F. J. (1939) *Proc. Roy. Soc. Med.*, 32, 308.  
 MAYO, C. W. Quoted by Finch, E. F. (1948) Personal communication.  
 STOECKEL, W. (1930) *Zbl. Gynäk.*, 54, 47.  
 TAUSSIG, F. J. (1941) *Amer. J. Roentgenol.*, 45, 813.

**Mr. J. B. Blaikley:** With the kind permission of my colleagues I have tried to analyse the results of treatment of carcinoma of the vulva at the Chelsea Hospital for Women and the Royal Cancer Hospital, for the years 1933 to 1943 inclusive. Owing to deficiencies in the follow-up a complete analysis was impossible, so I have confined myself to one or two aspects of treatment.

#### Results at Chelsea Hospital for Women :

|                                                 |    |    |    |     |
|-------------------------------------------------|----|----|----|-----|
| Total number of patients                        | .. | .. | .. | 29  |
| Five-year survival                              | .. | .. | .. | 11  |
| Five-year survival rate (relative)              | .. | .. | .. | 38% |
| The absolute survival rate cannot be calculated |    |    |    |     |

There were 14 earlier cases, with ulcers no bigger than 4 cm. diameter, and with no clinical evidence of involvement of the inguinal glands. Of these 10 were treated by excision or simple vulvectomy, 5 died (4 within two years) and one patient is untraced. All died of recurrent carcinoma. The survival rate after five years is only 40% among this group.

The remaining 4 early cases were treated by vulvectomy and inguinal lymphadenectomy (3 cases), deep X-rays to the glands (1 case). All 4 were alive at the end of five years.

#### The results at the Royal Cancer Hospital are similar:

|                                    |    |    |    |     |
|------------------------------------|----|----|----|-----|
| Total number of patients           | .. | .. | .. | 49  |
| Five-year survival                 | .. | .. | .. | 23  |
| Five-year survival rate (relative) | .. | .. | .. | 47% |
| (9 cases were untraced)            |    |    |    |     |

There were 16 cases with ulcers not bigger than 4 cm., and no clinical evidence of glands being involved. Of these, 8 were treated by simple excision of the vulva or some part of it: 4 were alive after five years and 4 had died, all 4 within two years; all died of recurrent carcinoma. The survival rate after five years is 50% of this group.

Of the remaining 8 cases, 2 were treated with radium only, neither can be traced. Of the other 6 cases, in 2 the inguinal glands were excised, in 2 telerradium was applied to the groins, and in 2 deep X-rays were given to the groins. All 6 were alive after five years.

If any further evidence were needed to condemn simple excision or vulvectomy, here it is. There is very little improvement in the five-year survival rate for these earlier cases on that for the total number of cases (all stages), whereas it ought to be considerable. The remaining patients have been treated in such a variety of ways that it is not possible to give useful figures.

Because only a few cases of carcinoma of the vulva are seen by any one gynaecologist each year, inadequate surgery is all too common. The choice of treatment lies between radical surgery or, if the patient is unfit, after excision of the vulva, telerradium may be applied to the groins. In actual fact few elderly women, with modern anaesthesia, are unfit for surgery. My experience is nothing like as great as Mr. Way's, but of recent years I have seen quite a few cases of carcinoma of the vulva. I do not consider that in the majority of cases it is necessary to remove the iliac glands, but it is necessary to make a complete

## Section of Ophthalmology

President—CHARLES GOULDEN, O.B.E., M.A., M.D., F.R.C.S.

[May 12, 1949]

**Ocular Defects in Still's Disease.**—H. E. HOBBS, F.R.C.S.

EYE defects were not described by Still (1897) when he first drew attention to the chronic infective arthritis of children which is now associated with his name; but, since that time, the clinical picture has been widely recognized and many observers have recorded associated ocular lesions, Uhthoff (1918), Ohm (1910), Fuchs (1918), Behmann (1921), Hauptvogel (1922), Waubke (1922), Friedländer (1933), Holm (1935), Wong (1941), Kurnick (1942), Gotfredsen (1949). Such defects, however, are rare incidents in the disease and hitherto no case appears to have been recorded in Great Britain.

D. M., a girl of 10, was admitted to the Royal Free Hospital under Dr. E. T. D. Fletcher in January of this year with a recurrence of pain in the knees and ankles. Still's disease was first diagnosed when she was aged 3, since when she has been almost continuously incapacitated. Although she is undersized her general condition is good and she is afebrile in spite of a persistently raised erythrocyte sedimentation rate (30 mm. in one hour). The mobility of the joints of the spinal column and extremities is seriously affected, although she is now without pain following a prolonged course of physiotherapy. In particular she is kyphotic, with very limited head extension. Movement of the joints of the limbs is restricted to a varying degree: in the knees and ankles markedly, in the fingers and wrists (which are swollen from periarticular changes) less so; the right elbow is ankylosed at 90 degrees. Radiographs show minimal bony changes.

Her eyes were first affected at the age of 4 and her visual acuity is now reduced to 6/36 in the right and 6/18 in the left, with glasses. Both corneæ show opacities in the interpalpebral area. Under the slit lamp these are seen to be localized in Bowman's membrane and the superficial corneal lamellæ and to have the faintly brownish turbidity with fenestrations characteristic of band-shaped opacities. In the right eye the opacity extends across the cornea whilst in the left the pupillary area is still clear. In both, near the limbus, appear small denser areas in which calcification appears to have begun. Both lenses show anterior subcapsular opacities and fine granular pigment deposits from old iridocyclitis. The pupils are mobile. The fundi show no abnormality.

A study of reported cases shows that a quiet chronic iritis productive of little disability is the usual, and may remain the only ocular lesion (Duke-Elder, 1940). Exudates, synechia and cataract are known to occur (Holm) and band-shaped corneal opacity has frequently followed within a few years (Holm, Kurnick). The prognosis for vision in these cases is much worse than in those with uncomplicated iritis.

In conclusion, I would like to thank my house surgeon, Mr. K. E. Read, for his assistance in looking up case notes at the Chelsea Hospital for Women, and Mr. R. Williams, registrar at the Royal Cancer Hospital, for looking up case notes of patients treated at that hospital.

**Mr. Alan Brews:** Of recent years I have been treating my operable cases of carcinoma of the vulva by a moderately radical excision of the whole vulva together with a block resection of the superficial and deep inguinal and femoral lymphatic nodes from both groins. I have performed this Basset type operation twelve times in all, on an average of two or three times a year, and the results have proved encouraging.

Under combined spinal and light general anaesthesia I have carried out the extensive dissection largely by cutting and coagulation diathermy. In removing all the inguinal and femoral lymphatic nodes I have always included the deep femoral gland of Cloquet but I have not, as yet, removed the external iliac glands. I have always removed the upper part of the internal saphenous vein.

After obtaining as complete hæmostasis as possible I have left the entire wound in both vulval and groin areas completely open and unsutured except for one stitch to prevent undue separation of the upper and the two lateral skin flaps. I insert a self-retaining catheter until the bowels act and I lightly pack the lower vagina with gauze soaked in flavine and liquid paraffin emulsion for forty-eight hours. A sterile towel is laid across the wound area and the bed-clothes are supported by an electric bed-cradle. No local treatment at all is given and exuding lymph is allowed to dry and cake on the wound surfaces. The area is kept at rest and physiotherapy is given to all other regions.

None of these patients has been got up for at least three weeks until the wound is covered by healthy granulations. The groin wounds heal completely in eight to ten weeks by linear scars. A feature of convalescence has been the complete absence of pain, and pyrexia due to secondary infection has been much less than with a closed wound.

The treatment of these cases should be developed in a limited number of centres so that all cases can be treated by an experienced surgical team and nursed by an equally experienced nursing staff.

**Mr. Clifford White** demonstrated sections from a specimen of so-called "non-ulcerating" carcinoma of the vulva. Clinically the case was apparently of low malignancy as the patient is alive and free from recurrence after six years although her very bad general condition imposed only a limited excision under local anaesthesia.

The growth was a prickle-cell carcinoma. Leucoplakia was not present.

Other speakers included Mr. A. P. Bentall, Dr. M. Lederman, Professor W. C. W. Nixon, Mr. Charles D. Read and Mr. J. A. Stallworthy.



The patient has been under fairly regular observation until the present time, and has had several partial excisions of the subconjunctival lipomas and one of the dermoids, for cosmetic reasons.

Ophthalmoscopic examination of the right eye was never very easy, but cataract was not noted. The fundus of the left eye was normal.

In December 1940 slit-lamp examination of the right eye showed slight opacity and vascularity of the deepest layers of the cornea, the centre part of the lens was swollen and opaque, the more transparent portion containing many white specks, some iridescent, and there were iridescent lines due to corrugations of the anterior capsule.

Four years later the conditions were similar, the visual acuity being "Fingers" in the right eye and 6/9 in the left. In December 1947 the right was painful, red and watery, as well as unsightly, and the patient, now fifteen years of age, asked to have it removed.

At this date the cornea was somewhat opaque, and details of the iris and anterior chamber were concealed, but the white bands crossing the anterior chamber seemed to have expanded and partly covered the coloboma. Subsequent microscopic examination showed that the deep opacity of the cornea was due to a pannus-like tissue anterior to Descemet's membrane, and that the pupil was obscured by complete opacity of the lens.

After excision, the eye was fixed in 10% formalin, and bisected equatorially.

The anterior half examined from behind (fig. 2) showed the lens opaque and

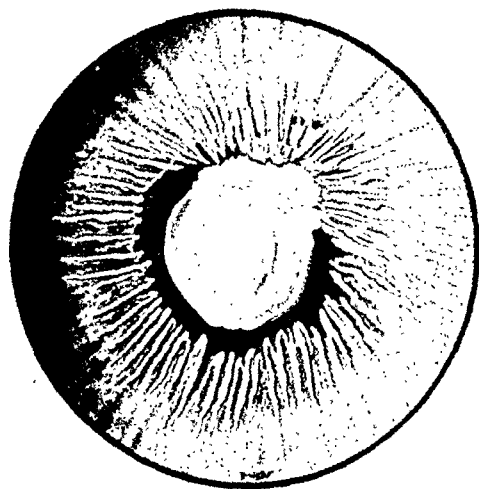


FIG. 2.—Anterior segment of the eye seen from behind. Shrunken and displaced lens. Coloboma of the iris above. Imperfectly developed ciliary processes in coloboma region. (From a coloured drawing by Mr. Gabriel Donald)

shrunken, with a particularly ragged margin in the coloboma area. In this region also (upper part of the figure) there was flattening of the ciliary processes, possibly congenital. In about half of its circumference the ciliary body was apparently normal, and normal iris could be seen in the same sector between the lens and the ciliary processes. The posterior half of the eye showed no abnormality.

Celloidin blocks were made, and sections cut antero-posteriorly. In the anterior segment the sections were approximately in the line of the iris coloboma.

#### HISTOLOGY

In fig. 3, a low-power view of the anterior part of the globe, many of the important features are visible. The section is not quite central, and one of the connective tissue bands is cut longitudinally, so that it is seen as a complete membrane crossing the chamber from side to side. In this section the iris at the lower nasal (L) side is adherent to the band by a broad synechia, and here the anterior chamber is separated by the band from the true angle.

The development of ocular lesions usually occurs early in the disease (in one of Friedländer's cases iritis preceded the appearance of joint symptoms by some six months), a fact which is in accordance with the modern view (summarized by Duke-Elder (1940), and referred to recently by Gotfredsen) that iritis in rheumatic conditions represents a separate ocular response to the infective agent causing the joint condition and should not be considered a secondary "rheumatic" manifestation.

## REFERENCES

- BEHMANN, A. (1921) *Klin. Mbl. Augenheilk.*, 66, 450.  
 DUKE-ELDER, W. S. (1940) *Textbook of Ophthalmology*, London, 3, 2155.  
 FRIEDLÄNDER, A. (1933) *Ugeskr. Laeg.*, 95, 1190.  
 FUCHS, E. (1918) *Klin. Mbl. Augenheilk.*, 61, 10.  
 GOTFREDSEN, E. (1949) *Brit. J. Ophthalm.*, 33, 261.  
 HAUPTVOGEL, J. (1922) *Klin. Mbl. Augenheilk.*, 69, 763.  
 HOLM, E. (1935) *Trans. Ophthal. Soc., U.K.*, 55, 478.  
 KURNICK, M. B. (1942) *Amer. J. Dis. Child.*, 63, 742.  
 OHM, J. (1910) *Klin. Mbl. Augenheilk.*, 48 (ii), 243.  
 STILL, G. F. (1897) *Med.-Chir. Trans.*, 80, 47.  
 UHTHOFF, W. (1918) *Klin. Mbl. Augenheilk.*, 60, 11.  
 WAUBKE, H. (1922) *Klin. Mbl. Augenheilk.*, 69, 79.  
 WONG, R. T. (1941) *Arch. Ophthalm.*, 26, 21.

## Multiple Congenital Anomalies of the Eyes

By A. J. BALLANTYNE, M.D. Glasgow

IN 1932 I described before this Section the case of a female infant, brought to the Glasgow Eye Infirmary with a history of swelling of the lids of the right eye at birth.

When I saw her for the first time, six days after birth, there was still some œdema of the lids, the cornea was a little cloudy, and focal illumination showed some K.P. and aqueous "flare". Under treatment with atropine and dionine the inflammatory signs disappeared.

The special interest in the case lay in the presence of a number of congenital abnormalities of the eyes, difficult to interpret and to bring into relation one to the other. In the right eye (fig. 1) these anomalies included: subconjunctival lipomata, dermoids

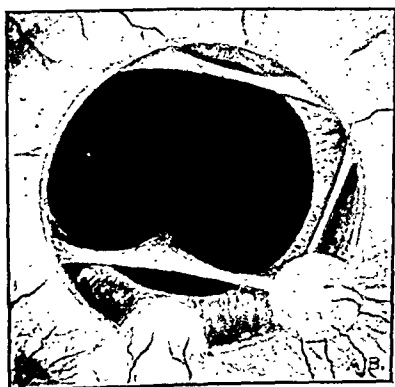


FIG. 1.—Clinical appearances a few days after birth. Subconjunctival lipoma and limbal dermoids. Coloboma of the iris. Glassy membranes crossing the anterior chamber.  $\times 4$ .

at the limbus, coloboma of the iris, and bands of white tissue crossing the anterior chamber. Also on the right side there was a small marginal coloboma of the right upper lid and a tiny pit at the junction of the right cheek and the ala nasi, while in the left eye there was a small anterior polar cataract with a remnant of the pupillary membrane attached to it. The normal prominence at the centre of the upper lip was a little elongated.

The lens presents, in some respects, the histological characters of a shrinking traumatic cataract. Some parts are in the process of breaking down into globular masses, some are composed of compact fibro-cellular tissue, some are hyaline and others calcified. Here and there the lens contains clusters of cells resembling the subcapsular epithelium, and where it is in contact with the sclero-cornea there are irregular masses of vascular fibrocellular tissue (fig. 6). Outside the lens capsule at its equator, there are several collections of inflammatory cells—lymphocytes, plasma cells, fibroblasts and endothelial cells. In some sections the lens has an irregularly dumb-bell shape due to absence of the nucleus. This appears to be an example of the developmental defect described as "disc-shaped cataract" by Collins (1898, 1908) and as "annular cataract" by von Szily (1938) which, however, is described as "hereditary and congenital, and always bilateral".

In the *posterior half of the globe* the papilla is seen to be somewhat prominent, but there is no lateral displacement of the retinal layers (fig. 7). The capillaries, especially

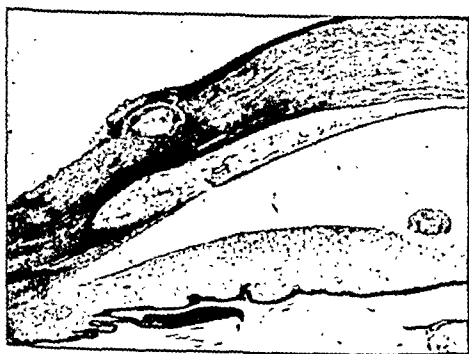


FIG. 4.—Angle of the anterior chamber at lower nasal side. Dermoid of the cornea. Deep lipoma in the sclero-cornea. A mesodermal band cut transversely.  $\times 10$ .

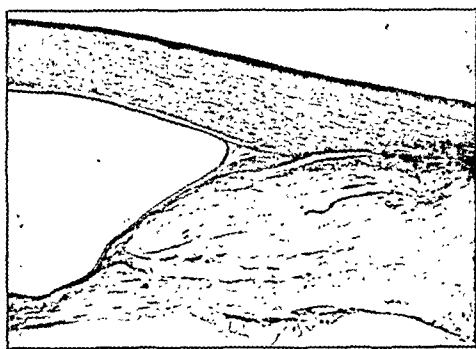


FIG. 5.—False angle at the upper temporal side. No trace of iris. False Descemet's membrane spreading on to surface of the lens.  $\times 10$ .

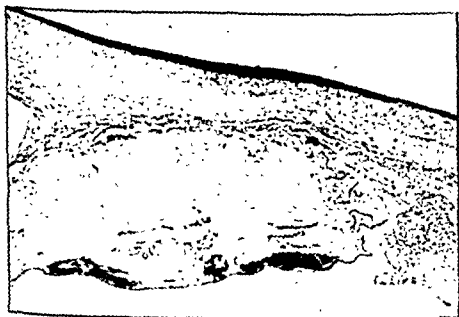


FIG. 6.—Lens cataractous, with calcification, displaced up and out and impacted in corneo-sclera. Chronic and acute inflammatory changes surrounding the lens.  $\times 10$ .

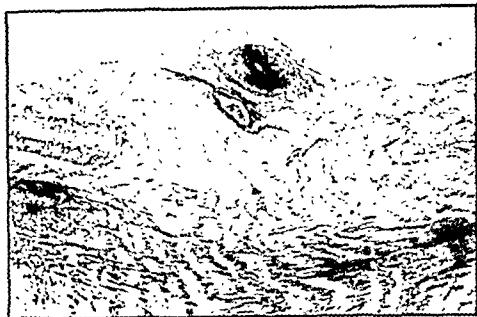


FIG. 7.—Antero-posterior section through the papilla. A large solid mass of elastic tissue causes a prominence on the anterior surface.  $\times 10$ .

those near the surface of the papilla, are wide and full. In and behind the lamina cribrosa for a distance of 2.5 mm. the central vessels are abnormally wide. The vein which has a maximum diameter of  $240\ \mu$  runs a fairly straight course, but the artery is tortuous and is cut transversely at several points in its course.

Just under the surface of the papilla at its centre (fig. 7) there is a round darkly staining body (purplish with Weigert's elastic tissue stain) about  $300\ \mu$  in diameter,

The central part of the cornea is normal in thickness and general structure, and at the lower nasal periphery it is greatly thickened, partly by the dermoid growth on its surface, and partly by a bulky mass of adipose tissue in its deeper layers. In sections through the point where one of the dermoids was excised the cornea is thin and its superficial layers are composed of scar tissue. The remaining dermoid consists of an

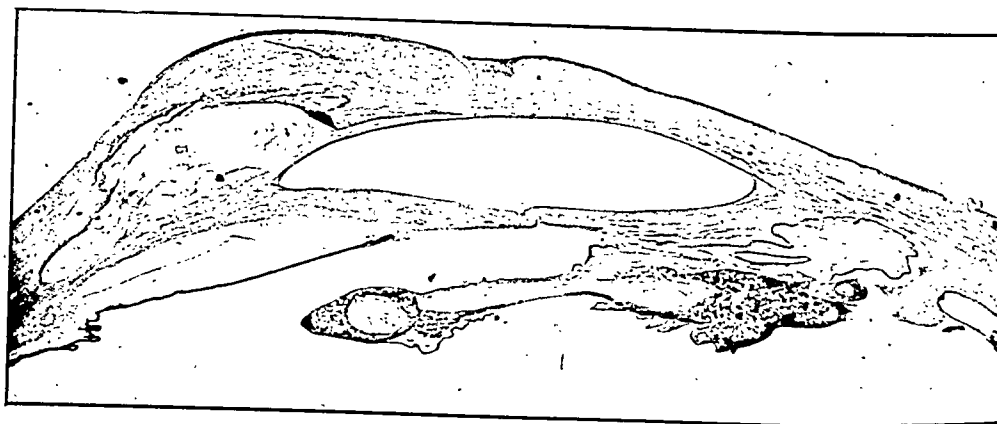


FIG. 3.—Anterior segment of the eye. Shows the superficial dermoid and deep lipoma near the limbus, mesodermal bands arising from the deepest layers of the corneo-sclera, displaced degenerate lens and coloboma of iris.  $\times 10$ .

implant of corneal epithelium (fig. 4). In parts it contains hair follicles, but there are no sweat glands and no cyst. The lipoma seems to be self-contained and in none of the sections is there any track connecting it with the subconjunctival tissues. On the opposite side, in some of the sections there is a thinner deposit of adipose tissue in the deepest layers of the corneo-sclera. The canal of Schlemm appears normal in those sections in which the lipoma occupies a relatively small part of the deep layers (fig. 4), but in many of the sections the lipoma extends into the situation normally occupied by the canal (fig. 3). The fibrous framework of the lipoma is in continuity with a layer of fibro-cellular tissue of varying thickness which spreads forward in front of Descemet's membrane towards the centre of the cornea. This no doubt accounted for the extensive opacity of the cornea observed clinically (figs. 3, 4).

Descemet's membrane and its endothelium are normal at the centre of the cornea, but at the lower nasal side where the iris is adherent to the cornea or the fibrous band leaves the cornea (fig. 3), Descemet's membrane is continued by a new membrane formation which lines the false angle and spreads on to the anterior surface of the iris or of the fibrous membrane. At the upper temporal side (the coloboma region) conditions are different. Here also there is a false angle formed by the cornea and one of the fibrous bands, where the latter is present (fig. 3) otherwise between the cornea and the lens (fig. 5). Descemet's membrane sweeps around the false angle and becomes continuous with, or is superimposed on, the lens, or extends on to the surface of one of the fibrous bands.

The condition of the lens is important. It is displaced in the upper temporal direction and its equator is impacted into a recess in the situation of the angle of the anterior chamber (figs. 3, 6). There is no trace of the iris in this situation, and no remnants of the tunica vasculosa lentis. The lens capsule forms a clear, highly tortuous line, apparently interrupted at some points, and in the region of the false angle it is difficult to trace. Here a new-formed glassy membrane, derived from Descemet's membrane, sweeps round the angle and seems to fuse with the anterior part of the lens capsule (fig. 5).

forms Descemet's membrane. Collins believed that such a failure of the development of the anterior chamber could be an impediment to the growth of the iris. So far, therefore, as the fibrous bands in the anterior chamber are concerned, the most satisfying explanation of their origin is that a fault in the splitting of the "post-endothelial mesoderm" destroyed the normal relationships of cornea and iris, leaving an incomplete diaphragm of mesoblastic tissue across the anterior chamber.

In our own case the conditions at the coloboma site do not suggest destruction of the iris, but rather a failure to develop. In view of the absence of evidence of perforation of the sclera, the cause of the displacement of the lens is not clear, but it is a feature which has been referred to in many of the complicated cases of developmental anomalies. The embryonic lens vesicle loses contact with the surface ectoderm at a very early stage (the second month in man), the iris and suspensory ligament begin to appear about the third month, but the formation of the anterior chamber by splitting of the mesoderm does not occur until the fifth month. Whatever the cause of the displacement of the lens may be, this could come about, and the lens take up its new position, before the rudiment of the iris appeared, and could thus inhibit the development of the iris in that situation.

It is to be expected that in the case under review the lens, acting as a foreign body, would set up a local irritation leading to inflammation of a mild type, which was active at the time of birth and was responsible for the vascular fibro-cellular tissue in and around the periphery of the lens. The *active* inflammation in the neighbourhood of the lens would probably account for the symptoms which led to excision of the eye.

We may take it then that at an early period of embryonic life there was a failure of the normal splitting of the mesodermal tissue which goes to form the structures surrounding the anterior chamber. This resulted in the formation of an incomplete diaphragm of mesodermal tissue in the form of glassy-looking bands crossing the anterior chamber from angle to angle and attached at several points to the cornea, iris and lens. Displacement of the lens in the upper temporal direction and its adhesion to the corneo-sclera inhibited the development of the iris in that segment. The lens was probably abnormal from the first, with a poorly developed nucleus, and by mechanical and chemical action set up a chronic inflammation in the adjacent sclera. Perforation of the capsule and invasion of the lens by fibroblasts would lead to further degenerative changes.

No explanation can be offered regarding the nature of the association of these lesions and the other congenital anomalies presented by this case—epibulbar dermoids, subconjunctival and deep corneal lipomata, colobomata of the skin and anterior polar cataract.

#### SUMMARY AND CONCLUSION

A clinical account of a case of multiple congenital anomalies of the eyes in an infant six days after birth was recorded in 1932 (Ballantyne, 1933), and the more affected eye was obtained for histological examination fifteen years later. At birth there were signs of iridocyclitis, which cleared up under treatment. The anomalies included coloboma of the right upper lid, subconjunctival lipoma, dermoids at the limbus, coloboma of the iris and bands of glassy-looking tissue crossing the anterior chamber from angle to angle and adhering at several points to cornea, iris and lens.

Microscopic sections brought out the following points: The limbal dermoids consisted of thickening and downgrowth of the corneal epithelium, with hair follicles but no sweat glands and no cyst formation. In some sections the dermoid had the appearance of an epithelial implant, which did not communicate with the surface epithelium. All round the limbus there was adipose tissue in the deepest layers of the corneo-sclera, and at the lower nasal side this constituted a bulky lipoma which showed no continuity with the subconjunctival lipoma. The tissue bands in the

like a ball of wool. In its centre there are two small lacunæ, 7 or 8  $\mu$  in diameter, each of which contains one red blood corpuscle. It thus resembles a vessel with a thickened wall composed entirely of elastic fibres, but it cannot be traced in continuity with any of the other vessels in this situation.

There is œdema in the posterior part of the retina and some cystic degeneration at the macula.

#### COMMENT

Cases at all closely resembling this one are apparently rather rare, and it is unusual to have the opportunity to make a histological examination after such a long period of clinical observation. Although at the date of the excision of the eye the cornea had become cloudy and the lens completely opaque, there is no reason to suppose that the intra-ocular conditions had undergone any substantial change in the interval.

Interest naturally centres in the nature and source of the bands of tissue crossing the anterior chamber. This problem and the relevant literature have been discussed by Ida Mann in "Developmental Abnormalities" (1937). To the naked eye the bands have an almost glassy appearance, and stretch across the chamber from angle to angle as if under some tension. Histologically they are mesodermal in origin, and resemble the sclera in their fibrous, acellular structure and in their staining reactions.

There are two possible explanations of the development of the bands: (1) that they are the product of an intra-ocular inflammation, and (2) that they are the result of a developmental fault; and there are several arguments in favour of the latter. In the first place the tissue is acellular and, even where one of the bands is adherent to the cornea or the iris, there is no sign of inflammation at the point of contact. In the second place an inflammation sufficiently intense to produce such a substantial "organized exudate" would have been much more destructive in its effects. Thirdly, the bands have no resemblance in their anatomical relations to the membranes resulting from known forms of endophthalmitis, and lastly, the membranes or bands are seen to emerge or split off from the deep layers of the sclero-cornea in front of the true angle of the anterior chamber.

At the same time there are evidences of inflammation in the coloboma region in the form of vascular scar tissue between the lens and the cornea, the formation of a false Descemet's membrane in the angle and on the surface of the lens, and the collections of inflammatory cells near the equator of the lens.

In the extensive literature of developmental anomalies there are numerous examples of multiple lesions, sometimes entirely ocular, sometimes associated with extra-ocular defects, as in the present case, and it is not uncommon to find, in the same case, inflammatory and non-inflammatory conditions. Von Hippel (1908) called attention to the tendency of colobomatous eyes to severe chronic inflammation and the formation of cataract, and van Duyse (1905) published a case in which coloboma of the eyelid was associated with "intra-uterine iridocyclitis".

Cases of antenatal dislocation of the lens, associated with coloboma of the iris, have been discussed by von Hippel (1908), Rindfleisch (1891), Manz (quoted by von Hippel) and others. Manz held that the developing lens remained too long in contact with the anterior segment of the eye, and thus impeded the development of the iris. Rindfleisch conceived that an antenatal inflammation led to a perforation of the sclera, loss of aqueous and impaction of the lens at the site of the perforation. In the present case no sign of perforation of the globe could be found.

Ida Mann discusses in some detail the group of cases in which hyaline bands are seen to cross the anterior chamber, in some cases with adhesions to the iris and cornea, and concludes that the underlying factor in these cases is faulty development of the post-endothelial tissue which lies between the surface epiblast and the lens at the 12 mm. stage in the human embryo. This tissue should normally form the iris stroma and pupillary membrane, and detaches itself from the mesoblastic layer which

# PROCEEDINGS *of the* ROYAL SOCIETY OF MEDICINE

ISSUED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE

HONORARY EDITORS

ERIC A. CROOK      E. R. CULLINAN

EDITOR

J. M. BROWNE KUTSCHBACH

G. S. W. ORGANE (Anæsthetics)

J. S. RICHARDSON (Clinical)

J. B. BROOKSBY (Comparative Medicine)

E. W. PROSSER THOMAS (Dermatology)

E. F. SCOWEN (Endocrinology)

ALLAN McFARLAN (Epidem. & State Med.)

A. C. WHITE (Exper. Med. & Therap.)

I. E. McCracken (History of Medicine)

W. A. MILL (Laryngology)

MAURICE DAVIDSON (Medicine)

J. St. C. ELKINGTON (Neurology)

LESLIE WILLIAMS (Obstetrics & Gynæcology)

B. W. FICKLING (Odontology)

F. T. RIDLEY (Ophthalmology)

H. L.-C. WOOD (Orthopædics)

C. S. HALLPIKE (Otology)

A. G. SIGNY (Pædiatrics)

F. R. SELBIE (Pathology)

M. B. RAY (Physical Medicine)

O. V. LLOYD-DAVIES (Proctology)

DENIS HILL (Psychiatry)

F. CAMPBELL GOLDING (Radiology)

CHARLES DONALD (Surgery)

G. M. FINDLAY (United Services)

A. CLIFFORD MORSON (Urology)

SECRETARY OF THE ROYAL SOCIETY OF MEDICINE

G. R. EDWARDS

anterior chamber, which might be described as an incomplete membrane, stretched across the anterior chamber from angle to angle, emerging from the deep surface of the corneo-sclera about the situation of the canal of Schlemm, and apparently in continuity with the deepest layers. At several points they were adherent to the iris and to the lens.

The lens was displaced up and out and impacted in a recess in the corneo-sclera. Absence of a nucleus gave it in some sections the shape of a dumb-bell.

At the site of the coloboma there was no trace of the iris, and sections showed no persistence of the tunica vasculosa lentis.

At some of the broad adhesions between the iris, cornea and mesodermal bands there was nothing to suggest an inflammatory reaction, but where the equator of the lens was adherent there was evidence of inflammation both old and recent. The mesodermal bands have no resemblance to persistent pupillary membrane or to the organized exudates resulting from endophthalmitis. Their origin is best explained by assuming a failure of the normal splitting of the mesoblast which forms the structures surrounding the anterior chamber, the bands belonging initially to the deep layers of the corneo-sclera and showing the same fibrillary structure and staining reactions.

The lens was probably abnormal from the beginning. The cause of its dislocation is not understood, but it seems justifiable to assume that if the embryonic lens was thus displaced before the appearance of the rudimentary iris it could cause complete inhibition of its growth at that point. It could also cause the chronic inflammation which was in progress at birth, and the acute inflammation which led to removal of the eye.

#### REFERENCES

- BALLANTYNE, A. J. (1933) *Proc. R. Soc. Med.*, 26, 313.  
 COLLINS, E. T. (1898) *Trans. Ophthal. Soc., U.K.*, 18, 124.  
 — (1908) *Ophthalmoscope*, 6, 669.  
 VON HIPPEL, E. (1908) in GRAEFE, A. and SAEMISCH, T., *Handbuch der gesamten Augenheilkunde*, Leipzig, 2, Abt. 1, Ch. 9.  
 MANN, I. (1937) *Developmental Abnormalities of the Eye*, Cambridge.  
 MANZ. (Quoted by von Hippel.)  
 RINDFLEISCH (1891) *Arch. Ophthal.*, 37, 192.  
 VAN DUYSE, M. (1905) *Encyclopédie Française d'Ophtalmologie*, Paris, 2, 368.  
 VON SZILY, A. (1938) *Trans. Ophthal. Soc. U.K.*, 58, 595.

Mr. Eugene Wolff said that he wanted to mention a small matter in connexion with the general pathology of the eye. Professor Ballantyne had said that because the iris was free of inflammatory cells it was a point against an inflammatory origin. He thought that argument had been raised a great many times. When Coats, for instance, said that he found no inflammatory cells in the choroid and therefore the choroid was not the cause of Coats' disease, that was an error. It was known that in a pseudo-glioma inflammatory cells might disappear entirely. The changes in the optic nerve suggested that there had been a uveitis. He did not think one could exclude the inflammatory theory.

Professor Ballantyne, in reply, said that he would not go so far as to claim that they could exclude the inflammatory theory, but he thought the facts were against it. How were they going to account for the tissue growing out of the corneo-sclera? Did Mr. Wolff suggest that uveitis could produce the tortuous vessels in the optic nerve? The inflammatory theory would need to explain not only the intra-ocular changes but the extra-ocular lesions, the coloboma of the eyelid and the congenital anomalies in the other eye.



# PROCEEDINGS

## OF THE

# ROYAL SOCIETY OF MEDICINE

Vol. XLII    No. 10    October 1949

## CONTENTS

Whole  
Proceedings  
Page

### Section of Proctology

|                                                          |     |
|----------------------------------------------------------|-----|
| DISCUSSION ON GRANULOMATA OF THE LARGE INTESTINE .. .. . | 763 |
|----------------------------------------------------------|-----|

### Section of Radiology

|                                                                                                                |     |
|----------------------------------------------------------------------------------------------------------------|-----|
| Carcinoma of the Lung.—President's Address by J. S. FULTON, C.B.E., T.D., M.D.,<br>F.R.C.P.Ed., F.F.R. .. .. . | 775 |
|----------------------------------------------------------------------------------------------------------------|-----|

### Section of the History of Medicine with Section of Odontology

JOINT DISCUSSION No. 2

C. E. WALLIS MEMORIAL LECTURE, 1948 [Number 4]

|                                                                                                                        |     |
|------------------------------------------------------------------------------------------------------------------------|-----|
| The Contributions of King's College, London, to the Science of Dentistry.—F. N.<br>DOUBLEDAY, F.D.S., M.R.C.S. .. .. . | 783 |
|------------------------------------------------------------------------------------------------------------------------|-----|

### Section of Neurology

MEETING AT THE MAIDA VALE HOSPITAL FOR NERVOUS DISEASES, LONDON, W.9

|                                                                                                                      |     |
|----------------------------------------------------------------------------------------------------------------------|-----|
| (1) Encephalo-Myelo-Radiculitis: A Chronic Form .. .. .                                                              | 791 |
| (2) Mid-Brain Syndrome in a Professional Boxer .. .. .                                                               | 792 |
| DOUGLAS MCALPINE, M.D., F.R.C.P., and FRANCIS PAGE, M.D., M.R.C.P.                                                   |     |
| (1) Multiple Cranial and Peripheral Neuropathy .. .. .                                                               | 793 |
| (2) Vestibular Syndrome with Facial Palsy .. .. .                                                                    | 793 |
| REDVERS IRONSIDE, F.R.C.P.                                                                                           |     |
| Primary Sensory Neuropathy.—S. NEVIN, M.D., and L. G. KILOH, M.B., M.R.C.P... ..                                     | 794 |
| Optic Atrophy. Diabetes Insipidus. Cause Undetermined.—W. RUSSELL BRAIN, D.M.                                        | 795 |
| Hereditary Optic Atrophy in Family with Keratoderma Palmaris et Plantaris<br>(Tylosis).—HELEN DIMSDALE, M.D. .. .. . | 796 |

### Section of Laryngology

|                                                                                                             |     |
|-------------------------------------------------------------------------------------------------------------|-----|
| The Present Position in the Surgical Treatment of Carcinoma of the Thoracic Gullet.—<br>C. P. WILSON.. .. . | 797 |
|-------------------------------------------------------------------------------------------------------------|-----|

### Section of Urology

|                                                                                                       |     |
|-------------------------------------------------------------------------------------------------------|-----|
| Management of the Patient with Anuria.—ASHTON MILLER, F.R.C.S. .. .. .                                | 801 |
| Observations on Familial Polycystic Disease of the Kidney.—J. D. FERGUSSON, M.D.,<br>F.R.C.S. .. .. . | 806 |

### Section of Odontology

|                                                                                  |     |
|----------------------------------------------------------------------------------|-----|
| The Sterilization of Carious Dentine.—J. L. HARDWICK, M.D.S... ..                | 815 |
| Penicillin in the Treatment of Dead Teeth.—W. G. CROSS, M.B., M.S., B.D.S. .. .. | 829 |

### Section of Orthopaedics

|                                                                         |     |
|-------------------------------------------------------------------------|-----|
| SYMPOSIUM ON RECONSTRUCTIVE SURGERY OF THE PARALYSED UPPER LIMB .. .. . | 831 |
|-------------------------------------------------------------------------|-----|

### Section of Endocrinology

|                                                                                                        |     |
|--------------------------------------------------------------------------------------------------------|-----|
| Radon Implantation for Acromegaly and Cushing's Syndrome.—D. W. C. NORTHFIELD,<br>M.S. .. .. .         | 845 |
| Radiotherapy in the Treatment of Pituitary Basophilism and Eosinophilism.—FRANK<br>ELLIS, M.D. .. .. . | 853 |



# MALE HORMONE

ROUSSEL

---

**TAB. METHYLTESTOSTERON. B.P.**

Glosso-Sterandryl—5, 10 and 25 mg.

**INJ. TESTOSTERON. PROP. B.P.**

Sterandryl—5, 10, 25, 50 and 100 mg.

**IMPLANT** of 100 mg. TESTOSTERONE

Sterandryl—Implant.



ROUSSEL LABORATORIES LIMITED  
4, Golden Square, London, W.1

GERrard 3111-2

## Section of Proctology

President—C. NAUNTON MORGAN, F.R.C.S.

[February 9, 1949]

### DISCUSSION ON GRANULOMATA OF THE LARGE INTESTINE

Mr. V. Zachary Cope: *Actinomycosis Involving the Rectum and Colon.*

Actinomycosis occurs so seldom in the rectum and colon that no surgeon, either proctologist or general, is likely in a lifetime to see more than a few cases. How rare it is may be judged by the very few cases found in the records of hospitals entirely devoted to diseases of the rectum. Only two cases could be culled from the records of St. Mark's Hospital in London. It is also noteworthy that in several cases in the literature the correct diagnosis was not made during life, and that fact is a sufficient justification for its special consideration.

You will note that my title is not "actinomycosis of the rectum and colon" but "actinomycosis involving the rectum and colon" for, as we shall see, the disease does not so much attack the bowel as the tissues round the bowel. This was well shown in the case recorded by Yeomans where the involvement of the peri-rectal tissues was more obvious than that of the wall of the rectum itself.

For a proper understanding of the changes wrought in the rectal and colonic regions by actinomycosis it is essential that the main pathological features of the disease should be outlined. There are many varieties of actinomyces, some aerobic, some anaerobic. The common type which grows on grasses and grains will grow readily in the air but the type which commonly causes pathological lesions in the cow and in man is anaerobic or at least micro-aerophilic. The aerobic form is frequently saprophytic and can easily be cultured but the pathogenic form is difficult to culture and the organism is easily killed by drying. The common pathogenic form, *Actinomyces bovis* of Wolff-Israel, is often resident in carious teeth but has never been found outside the body. It must be admitted, however, that on rare occasions the aerobic form of actinomyces does become pathogenic, but this fact does not justify us in thinking that the sucking of straws at the one end or the wiping of the parts with hay at the other end of the alimentary canal is often if ever the method of infection.

Far and away the most common mode of entry of the fungus into the body is through the lining of the alimentary canal, but the lungs, skin and possibly the female genital canal are occasional routes of entry. More than half the cases of actinomycosis occur in the facial region or in the neck as a direct infection from the mouth or pharynx.

**Copyright:** The Society holds the copyright of all matter accepted for publication in the *Proceedings*. Requests for subsequent publication elsewhere should be made to the Honorary Editors. All papers, &c., presented at meetings (other than those which have been previously published) are held to be subject to the Society's copyright until a decision in regard to their publication has been made.

**Digests:** Requests for permission to make Digests from the *Proceedings* should be addressed to the Honorary Editors.

All communications concerning Editorial Business should be addressed to  
THE HONORARY EDITORS, 1, WIMPOLE STREET, LONDON, W.1

Applications for advertisement space in the "*Proceedings*" should be made to the Society's official advertising agents, Messrs. C. Mitchell & Co. Ltd., Mitchell House, 1 and 2, Snow Hill, London, E.C.1.

Copies of the whole *Proceedings* may be purchased through any bookseller. Prices are as follows:—

|                                                                     |                           |
|---------------------------------------------------------------------|---------------------------|
| Single copies .. .. .                                               | 10s. 6d. each, post free. |
| Annual subscription, covering 12 monthly issues and annual index .. | £6 6s. 0d.                |

Reprints of Sectional parts may be obtained direct from the Society. Prices are as follows:—

|                             |                          |
|-----------------------------|--------------------------|
| Single copies .. .. .       | 3s. 6d. each, post free. |
| Annual subscription .. .. . | 15s. 0d.                 |

Fellows and Members of the Royal Society of Medicine are asked to apply direct to the Society for any copies of the *Proceedings* they may require, whether whole or Sectional, in addition to those they receive *gratis*. Prices are as follows:—

**Whole *Proceedings*:**

|                                                            |                          |
|------------------------------------------------------------|--------------------------|
| Single copies .. .. .                                      | 7s. 6d. each, post free. |
| Complete volume (12 monthly issues and annual index) .. .. | £5 0s. 0d.               |

**Sectional *Proceedings*:**

|                             |                          |
|-----------------------------|--------------------------|
| Single copies .. .. .       | 3s. 0d. each, post free. |
| Annual subscription .. .. . | 10s. 0d.                 |

## LEWIS'S BOOKS

### EUGENE WOLFF'S ANATOMY OF THE EYE AND ORBIT

Third Edition. 323 illus. (21 coloured). Cr. 4to. 45s. net.

### GABRIEL'S PRINCIPLES AND PRACTICE OF RECTAL SURGERY

Fourth Edition. Revised with 11 coloured plates and 278 other illus. Royal 8vo. 45s. net.

### WESTON'S SIGHT, LIGHT AND EFFICIENCY

With illustrations. Royal 8vo. 42s. net. (Just published.)

### MACLEOD AND MUENDE'S PRACTICAL HANDBOOK OF THE PATHOLOGY OF THE SKIN

Third Edition, with illustrations (some coloured). Royal 8vo. 50s. net. Reprint 1948.

### LYLE AND JACKSON'S PRACTICAL ORTHOPEDICS IN THE TREATMENT OF SQUINT AND OTHER ANOMALIES OF BINOCULAR VISION

Third Edition. With 151 illus., including 3 coloured plates. Crown 4to. 35s. net, postage 9d.

### ROXBURGH'S COMMON SKIN DISEASES

Eighth Edition, with 8 coloured plates and 212 illustrations in the text. Demy 8vo. 21s. net, postage 9d.

### ROBERTS' CHRONIC STRUCTURAL LOW BACKACHE DUE TO LOW BACK STRUCTURAL DERANGEMENT

With 137 illustrations on 46 plates. Crown 4to. 45s. net.

### STRACHAN'S TEXTBOOK OF OBSTETRICS

With 3 coloured plates and 323 other illustrations. Royal 8vo. 45s. net.

### BARTON HALL'S PSYCHOLOGICAL ASPECTS OF CLINICAL MEDICINE

With illustrations. Demy 8vo. 21s. net, postage 9d.

Lewis's publications are obtainable of all Booksellers.

LONDON: H. K. LEWIS & Co. Ltd.  
Telephone: EUston 4282 (5 lines)

## H. K. LEWIS & Co. Ltd.

### MEDICAL AND SCIENTIFIC BOOKSELLERS

Large stock of works in all branches of Medicine, Surgery and Science always available. Catalogues on request. Please state your particular interest.

### FOREIGN BOOKS

Select stock. Books obtained from abroad under Board of Trade Licence.

### MEDICAL AND SCIENTIFIC LENDING LIBRARY

Annual Subscription from One Guinea.

Special Terms to Students at the London and Provincial Medical Schools. Prospectus post free on request. Bi-monthly list of new books and new editions sent post free on request.

### THE LIBRARY CATALOGUE

Revised to December, 1943, containing classified index of authors and subjects. To subscribers: 12s. 6d. net; to non-subscribers: 25s. net; postage 9d. Supplement 1944 to December, 1946. Demy 8vo. Pp. viii + 168. To subscribers: 2s. 6d. net; to non-subscribers: 5s. net; postage 4d.

### SECONDHAND DEPT.: 140 GOWER STREET, W.C.1

A large stock of Scientific and Technical books on view. Standard works and recent editions. Libraries or small collections bought.

### STATIONERY DEPT.

Note-books, loose-leaf, or bound, writing pads, fountain pens, pencils, plain or coloured.

LONDON: 136 GOWER STREET, W.C.1.  
Business hours: 9 a.m. to 5 p.m., Saturdays to 1 p.m.

cases of secondary actinomycosis in which the infection came from another part of the abdomen. It is sufficient to recognize primary and secondary cases. From the literature and from personal enquiries I have collected a series of 40 cases in which the rectum has been involved in actinomycosis. From a survey of details provided (and they were in many cases very inadequate) one can make the rough conjecture that *one-half of the cases began with a primary lesion arising in the ampulla of the rectum*, and the other half resulted from a secondary involvement of the rectum. In some cases the disease was so widespread that it was quite impossible to make a guess as to the source of origin.

In this group of cases there were considerably more males than females—a feature which is characteristic of actinomycosis in all parts of the body. The age of the patients varied from 14 to 70 but the commonest age-incidence was from 20 to 40.

It is not surprising that the actinomyces should cause lesions around the anal canal and ampulla of the rectum. Indeed it is strange that these lesions are not more common. The organism must very often dwell in the rectal ampulla for it resides frequently in the cæcum and appendix; minute traumata of the rectal mucosa must be fairly common, and secondary infection would be at hand to encourage any infective process. That it is rare must point to the development of some local immunity.

*Primary.*—Melchior rightly points out that lesions having their origin in the rectal ampulla or anal canal present several characteristic features. The disease starts as a local peri-anal or ischio-rectal abscess which bursts spontaneously; it is almost always subacute or chronic, the process tends to spread backwards and laterally rather than forwards and often extends through the sacro-sciatic foramen to the gluteal region. He might have added that the diagnosis is almost always made at a late stage unless—as in the cases recorded by Poncet—the observer has a special interest in or experience of actinomycosis. Occasionally abscess formation may be late and the chief lesion will then be a massive formation of hard, wooden connective tissue by the side of the rectum. Rarely the original peri-anal abscess may be more acute and painful but it soon becomes chronic. The duration of the disease varies greatly. It may run its course in two or twenty years. There may be apparently great improvement, yet at a later date severe recurrence may take place. In one remarkable case of Poncet's carcinoma developed at the site of the disease after many years.

The diagnosis of primary rectal actinomycosis can only be made with certainty by identification of the fungus in the discharge; usually the characteristic granules give one the clue. The disease may closely simulate malignancy, tuberculosis, syphilis or sepsis and one must always be on the look out for it. It is seldom that the sigmoidoscope has revealed it, though the wonderful case of Sir Gordon Gordon-Taylor's was an exception.

The prognosis of primary actinomycosis of the rectum has up to the present been bad. In the case-reports which give full details only four instances of apparent or prospective cure appear—those of Melchior, König, Risak, and Steenrod. Even in these cases one could not be certain that recurrence might not take place, for the after-history of the cases of König and Risak is not given and slight sinuses still remained at the time of reporting in the cases of Melchior and Steenrod.

The case recorded by Risak deserves special mention. In this case actinomycosis developed after an excision of the rectum for carcinoma in which a sacral anus had been left. The patient presented himself a year later complaining of incontinence, so the stump of the anal canal was anastomosed to the freed sacral anus. In the thick tissue which intervened between the two parts of the bowel it was found that there was a focus of actinomycosis. It seems most likely that the infection had taken place at the time of the primary operation and had slowly developed. The suggestion made

Next to the mouth-region the cæcum and vermiform appendix are the most frequent sites for actinomycosis. The clinical course of such cases is well known, but I must emphasize the fact that the symptoms of appendicitis may be minimal and the inflammatory process in the appendix masked by the remote lesions of actinomycosis. The pathological process develops more on the outside of the bowel rather than in the bowel-wall and often forms a mass in the adjacent mesentery. In such cases there may be a scar to show where the fungus has broken through the wall but often there is not even this indication. When in case-accounts we are informed that there was an opening into the rectum or colon communicating with an abscess this is more likely to be due to the secondary bursting of an abscess into the lumen rather than an indication of the route of entry of the fungus into the tissues of the body. In many recorded cases this mistake has been made.

With regard to the colon as a site for actinomycosis—I shall only mention those few cases in which the lesion was so limited to a certain area of the bowel that it might be concluded that it had its origin there; it would serve no useful purpose to mention all those cases in which one or other part of the colon had been secondarily affected by an extensive abdominal focus of the disease.

I have only been able to collect 6 cases to which the term primary *actinomycosis of the colon* might reasonably be applied.<sup>1</sup> They are the cases which were under the care of Pannett, Matyas, König, Querneau, Duttman and myself. In 4 of these cases the actinomycotic mass was excised under the impression that it was a malignant tumour. In a fifth the huge tumour was thought to be an inoperable malignant mass. The sixth case, of which I was unable to get full records, involved the transverse colon and also involved the stomach. The other 5 cases involved the sigmoid region. The details of the cases make very interesting reading. The case which came under my own observation was that of a middle-aged man who had been operated upon before he came to me, and the surgeon who operated had considered that he had to deal with an inoperable tumour of the sigmoid; he therefore closed the abdomen. The patient was seen by other surgeons who advised X-ray treatment. A sinus formed, however, and the actinomyces were found. When I saw him there was a large mass in the left lower abdomen. This diminished under treatment with penicillin but a faecal fistula formed, the liver enlarged and ultimately a large hepatic abscess burst through the diaphragm and the lungs became involved. From this condition he almost died but massive doses of penicillin caused great improvement though bronchiectasis developed and actinomyces were still obtainable from the sputum. Later a left cerebral abscess developed and was excised by Sir Hugh Cairns but the only organisms found in this abscess were diphtheroids. The patient is at present in fairly good health though his right arm is still weak. The abdominal tumour completely disappeared and the faecal fistula closed up.

We now come to *actinomycosis involving the rectum* which may present many diagnostic puzzles to the surgeon. The condition is seldom diagnosed till late in its course, and that for a variety of reasons—secondary infection may mask the actinomyces, the chronic inflammatory tissue may easily simulate malignant disease, and it may need the cutting of many sections to show the invading parasite. Most important of all, the surgeon may not even think of actinomycosis as a possible lesion in that position.

Melchior divided cases of rectal actinomycosis into primary, in which the infection came from the lumen of the rectum, and secondary, in which it reached the rectum from a focus elsewhere. He divided the primary cases into upper and lower according to that part of the rectum in which infection was thought to have taken place. This subdivision is in my opinion unnecessary for the upper group were almost certainly

<sup>1</sup> Since this paper was written there have been 2 recent cases of actinomycosis of the colon recorded by E. M. Farris and R. V. Douglas in *Archives of Surgery* (1947), 54, 434.

The methods of differential diagnosis necessary to distinguish actinomycosis from syphilis, tuberculosis, amœbiasis, malignant disease and chronic pyogenic conditions need not be fully discussed here for they are all part of routine work. The only certain positive diagnosis, however, is by the finding of the organism, usually in the little granules which are easily seen in the pus. In those cases which do not soften soon but remain as hard masses of connective tissue it will be necessary either to wait a long time for the ultimate softening, or to examine under the microscope part of an excised mass. Even then it may require many sections to show the characteristic fungus.

It is well always to make an attempt to culture the organism, and one must beware of being misled by the occurrence of an occasional filament of a saprophytic actinomyces in the pus. There are no reliable blood-tests for infection by actinomyces and in my list of cases I have excluded several in which the only indication of the disease was a blood-reaction.

*Treatment.*—The outlook for patients suffering from rectal actinomycosis has until recently been grim. Most of them have succumbed sooner or later. The number of recorded cures can be counted on the fingers of one hand. The methods of treatment have been many and various. Potassium iodide has been the sheet anchor in spite of its not being a true specific; it certainly softens and helps to get rid of the inflammatory tissue but it does not cure. In any case there is no need to give the large doses usually prescribed. 10 grains t.d.s. in a glass of milk should be sufficient. Five or ten drops of tincture of iodine in the same medium is also good.

The other useful method of treatment is radiation by either intensive or graduated doses of X-rays. In a few cases radium has been of benefit. Antiseptics such as copper sulphate, formalin and the rest are mentioned only to condemn. Vaccines and sera are of little avail. Lately the sulphonamide group of drugs has proved of some use both to combat secondary septic infection and for their direct action on the actinomyces.

The actinomyces is fortunately sensitive to penicillin. In the course of the last two or three years I have had the pleasure of seeing this effect clinically demonstrated on desperate cases which would formerly have held out not the slightest hope of recovery. It must be given in large doses for long periods of time; a short intensive course is of little use. The patient should be given about half a million or a million units daily for a period of two or three months without an interval of cessation. The method of giving it need not be discussed here but I favour one or two big doses in the twenty-four hours, given intramuscularly. A little local anæsthetic should be combined with the injection to lessen discomfort.

By this new drug we have, at length, a reasonable prospect of curing that interesting but formerly fell disease whether affecting the face or the rectum.

#### BIBLIOGRAPHY

(These references are given according to the date of publication of the cases)

- ZEMANN, A. (1883) *Med. Jber. Wien.*, 477.  
 MIDDELDORPF, K. (1884) *Dtsch. med. Wschr.*, 10, 225.  
 ROTTER, (1886) *Verh. dtsch. Ges. Chir.*, 15, 105.  
 GEISSLER-JÄNICKE (1889) *Bresl. ärzt. Z.*, 11, 58 (2 cases); abstracted in GRILL, A. (1895).  
 SCHARTAU, H. F. (1890) Ein Beitrag zur Kenntniss der Aktinomykose (Inaug. Diss.). Kiel.  
 BARTH, A. (1890) *Dtsch. med. Wschr.*, 16, 742.  
 HESSE, G. (1892) *Dtsch. Z. Chir.*, 34, 275.  
 RANSOM, W. B. (1892) *Med.-chir. Trans.*, 75, 85.  
 SANTER, E. O. (1892) *Arch. klin. Chir.*, 43, 257.  
 ORB, M. (1892) Zur Casuistik der Actinomykose (Inaug. Diss., Erlangen). Berlin.  
 MÜLLER, K. A. See GRILL, A. (1895).  
 GRILL, A. (1895) *Beitr. klin. Chir.*, 13, 551.  
 BECK, v. (1901) *Ärzt. Mitt. Baden*, No. 1 u. 2; abstracted in *Zbl. Chir.* (1901) 28, 331.  
 THEVENOT, L. (1902) *Rev. Chir., Paris*, 26, 250 (2 cases by Poncet).  
 PONCET, A. (1903) *Gaz. Hôp., Paris*, 76, 325.  
 BEVAN, A. D. (1905) *Ann. Surg.*, 41, 641.

by Risak that contamination of the wound (which was not quite healed when the patient left hospital) could have occurred from the grass which he might have used to wipe the parts round the anus does not bear scrutiny; and infection from the unused anus would be most unlikely.

By *Secondary Actinomycosis* of the rectum we mean those cases in which the disease spreads from a focus elsewhere in the abdomen. This primary focus is most commonly the appendix, but there are several cases in which the rectum was invaded secondarily to the ovaries which of course may possibly have been infected in the first place from the appendix. Finally there is one interesting case in which the rectal disease was secondary to the perforation of a gastric ulcer, which presumably gave the opportunity for the fungus to escape and drop down to the pouch of Douglas. There are a few cases in which it appeared likely that the fungus might have escaped from the iliac colon but this is mere speculation.

The characteristic feature of most of the secondary cases is the definite history of an attack of acute abdominal pain with fever and occasionally vomiting some time prior to the onset of the rectal symptoms. The time-interval between the acute abdominal crisis and the secondary rectal symptoms has usually been from three to six months. It is interesting to recall that Melchior, in describing cases in which he thought primary infection occurred high up in the rectum, expressed himself as puzzled to account for the previous occurrence of acute symptoms indicative of peritonitis; he did not appreciate the probability that these were in reality secondary cases following the escape of the fungus from another part of the bowel. I have already mentioned that it is not unknown for the site of entry or escape to heal up completely. In Barth's case the illness started with tenesmus and the passage of mucus followed by acute abdominal pains and fever and a lower abdominal abscess. At the autopsy fifteen months later the rectum was fixed in a mass of hard actinomycotic tissue and the 10 cm. long appendix which contained a soft concretion was firmly adherent by its tip to the rectum, and there was found a communication between the lumen of the rectum and that of the appendix by a narrow channel at the site of adhesion. Here there can be little doubt that the primary infection was through a perforation of an acutely inflamed appendix. The appendix at the time of autopsy was free from all signs of disease.

There have been several recorded cases of actinomycosis developing round the site of perforation of a gastric ulcer, and in one case the fungus was found actually in the wall of the stomach at the site of perforation, but the only recorded case in which rectal actinomycosis was secondary to perforation of a peptic ulcer was that reported by Gordon-Taylor. Here the occurrence of obstructive symptoms and the finding of a mass bulging into the anterior wall of the upper rectum was very puzzling and the possibility was even considered of it being due to a retained swab. Exploration proved this to be out of the question but the true diagnosis was only demonstrated when secondary actinomycotic abscesses of the liver were opened and typical granules found.

*Symptoms.*—A patient suffering from actinomycosis of the rectum may come to the proctologist with one of the following symptoms: Pus, muco-pus, or mucus in the stools; diarrhoea, constipation or diarrhoea alternating with constipation; supuration by the side of the rectum or anus; obstruction of the large bowel with abdominal distension; piles or fistula; or it may be that in a routine examination of a patient with low abdominal tumour a swelling may be found bulging into the rectum on its anterior, lateral or even posterior wall, or maybe all round it. Such a diversity of possible symptoms shows that there is nothing truly characteristic, and points the moral that one should always entertain the possibility of actinomycosis in any difficult or doubtful case.



An extra-rectal inflammatory mass is by no means an uncommon complication of advanced Crohn's disease when the primary lesion occupies its usual site in the terminal ileum. For this reason the literature now contains a considerable number of reports of such cases complicated by peri-anal abscess and ulceration and by anal fistula. In a small number of such cases it was a proctological complication which brought the patient to the surgeon for the first time.

Returning to the difficult subject of Crohn's disease occurring as a primary lesion in the colon, I should like to recount my own experience. For some years I could not satisfy myself that the specimens I examined contained the submucous lesion in a typical form. Since then I have examined three specimens in which the classical submucous lymphatic hyperplasia with non-caseating giant-cell systems was present, together with a striking degree of submucous lymphædema. My own experience is too small to be dogmatic regarding the site of election of the disease in the large bowel but I have a strong impression that it tends to affect the transverse colon and none of the specimens I have seen was a primary growth in the sigmoid.

**Mr. David H. Patey:** Crohn's disease is not a common disease and, apart from a few surgeons and surgical clinics which have made a special study of the subject, most surgeons' experience is limited to the occasional case stumbled on during the course of routine abdominal surgery. My own experience is of the latter limited type, but I have noted a few small points which may or may not be of some significance and which I thought might be worth mentioning, in case others with more knowledge and experience than myself might have come across something of the same kind. In 2 cases while estimating the feasibility of a resection I measured the total length of small intestine (jejunum and ileum) and in 1 case found it was  $7\frac{1}{2}$  feet and in the other 9 feet. In the latter case, a resection of up to 4 feet was stated to have been previously performed, but even so the length of intestine was well below the average. Is there any information about the length of the small intestine in cases of Crohn's disease? In one of the cases there was associated with the disease a wedge-shaped induration of the mesentery of the ileum, the long axis of which corresponded to the line of the main blood supply as if a vascular factor might be concerned. Another point that I have to make is that in this same case there was marked spasm both of the pylorus and of the colon, particularly the pelvic colon, which showed multiple contracted spastic segments. Has this observation any significance in view of the suggested relationship between Crohn's disease and ulcerative colitis? And finally, have other surgeons met with a familial tendency to this disease?

**Mr. R. W. Nevin:** Amœbic Granuloma.

*Introduction.*—The importance of intestinal amœbiasis to the surgeon is that the condition may simulate almost any abdominal lesion and if operation is carried out in unrecognized and unsuspected cases the mortality is very high. Surgical incisions in these cases heal with difficulty and may become the site of an ulcerative process. In fact, it has been said that this condition is one with a surgical diagnosis and a medical treatment.

The large number of Service personnel who have served in countries where amœbiasis is endemic and have now returned make this subject of great practical importance.

An unusual manifestation of the infection in the bowel is the formation of a granuloma. This is most commonly found either in the cæcum or in the rectosigmoid region. This hypertrophic lesion chiefly affects the submucosa and consists of round-celled infiltration with lymphoid hyperplasia and a number of histiocytes and eosinophils. A granuloma is very easily confused with carcinoma. A mass is felt and a partial or complete obstruction may be present. Mistakes are frequently made in diagnosis

- NOVÉ-JOSSERAND, L. (1907) *Lyon méd.*, 108, 989.  
 POPOV (1909) *Russk. Vrach.*, No. 14; abstracted in *Dtsch. med. Wschr.* (1909) 35 (i), 812.  
 GUDER-FEURER. See KROEBER, W. (1909).  
 KROEBER, W. (1909) Über Einengung des Rektums durch aktinomykotisches Exsudat (Inaug. Diss.). Leipzig.  
 MELCHIOR, E. (1910) *Beitr. klin. Chir.*, 70, 722 (2 cases).  
 KÖNIG, F. (1913) *Mitt. Grenzgeb. Med. Chir.*, 25, 119.  
 KAZDA, F. (1920) *Dtsch. Z. Chir.*, 156, 312.  
 RISAK, E. (1927) *Dtsch. Z. Chir.*, 205, 129.  
 KAUFMANN, E. (1929) Pathology for Students and Practitioners. Tr. by S. P. Reimann. London, 2, 842.  
 BARTSCH, G. H. (1931) *Wien. klin. Wschr.*, 44, 170.  
 BENSAUDE, R. (1933) *Pr. méd.*, 41, 371.  
 PERRY, C. C. (1935) *Trans. Amer. proctol. Soc.*, 36, 196.  
 YEOMANS, F. C. (1936) Proctology. New York. 2nd edn., p. 342.  
 QUERNEAU, J. (1936) *Mém. Acad. Chir.*, 62, 369.  
 GORDON-TAYLOR, G. See COPE, V. Z. (1938) p. 101 and Plate IV, facing p. 112 (2 cases).  
 PANNETT, C. A. See COPE, V. Z. (1938) p. 111.  
 COPE, V. Z. (1938) Actinomycosis. London.  
 VONNESSEN, O. (1939) *Zbl. Gynäk.*, 63, 754.  
 MATYAS, M. (1939) *Arch. klin. Chir.*, 195, 687.  
 AUSTER, L. S. (1940) *Amer. J. clin. Path.*, 10, 652.  
 STEENROD, E. J. (1940) *Amer. J. Surg.*, 48, 567.  
 DUTTMAN (1941) *Zbl. Chir.*, 68, 581.  
 PERRY, A. C. (1941) Personal communication.  
 BUBIS, J. L. (1945) *Med. Times, N.Y.*, 73, 227 (2 cases).  
 BUTLER, E. C. B. (1949) *Proc. R. Soc. Med.*, 42, 768.

**Mr. E. C. B. Butler:** In the last 24 cases of actinomycosis of the colon and rectum admitted to the London Hospital 2 have been rectal in origin. The first case presented as an ischio-rectal abscess; this was drained and later a track excised. The condition was healed in twelve months and the man has remained well since.

The second case was a woman aged 33.

For thirty months she had been treated for osteomyelitis of the pelvis and arthritis of the hip. The cause was supposed to be the *Staphylococcus aureus*.

1.1.43: She was admitted to the London Hospital because of persistent discharge from her pelvis. Culture showed actinomyces.

She was given iodides by mouth and repeated X-ray therapy. She was readmitted several times until her last admission in 1945 when she died of amyloid disease.

*Post-mortem.*—Primary focus of peri-rectal actinomycosis with sinuses affecting the pelvic bones and diffuse amyloid disease.

In the 22 cases of infection of the caecal region there were 11 deaths; 1 of the fatal cases had also an extensive carcinoma of the ascending colon.

#### Professor G. Hadfield: Crohn's Disease.

Although Crohn in his original description laid no stress on the occurrence of regional ileitis in the large intestine, cases in which the disease attacks the colon are no longer rarities. The lesion is usually in continuity with a primary focus in the terminal ileum but may follow excision of an ileal lesion as a recurrence. A primary lesion in the colon is uncommon. Whatever its origin, the colonic lesion shows far less tendency to diffuse infiltration than the ileal lesion and tends strongly to be localized, projecting and tumour-like. It is, in addition, far less clinically outspoken and by the time the specimen reaches the pathologist the submucous non-caseating lymphatic hyperplasia peculiar to Crohn's disease is largely destroyed by secondary ulceration and surface infection.

*Operation.*—Cause of obstruction was a thick œdematous band in the right iliac fossa. This was divided. After operation, improved slowly.

21.12.42: Further course of emetine and amibarson.

18.1.43: No exudate, amœbæ or cysts in six successive stools.

4.2.43: Evacuated to U.K. Fit.

II.—In Iraq a young soldier presented with a mass in the right iliac fossa, which was discrete and slightly tender; he had *Entamœba histolytica* in his stools. The lesions cleared up on emetine.

III.—A woman, aged 46, who was seen in Out-Patients in London and who had never been out of England, gave a history typical of carcinoma of the rectum and on examination with a finger there was a firm fixed mass in the upper third of the rectum. Proctoscopy and sigmoidoscopy revealed no ulcers or abnormalities other than the palpable lesion, which was ulcerated and protruded into the lumen of the rectum and involved about two-thirds of its circumference. A clinical diagnosis of carcinoma of the rectum was made but a specimen taken for biopsy was returned as granulation tissue. A further biopsy confirmed this. The stools were searched for amœbæ which were found. The mass disappeared completely on a course of emetine.

IV.—D. W., aged 42, was admitted to St. Thomas's Hospital on February 2, 1948, complaining of abdominal pain, diarrhœa and backache for five months with loss of 10 lb. in weight.

Two years previously he had returned to England after three years' service in Burma. While in Burma he had had one attack of stomach pains and diarrhœa, which lasted for three weeks, but he had never been investigated.

A diagnosis of carcinoma of the rectum was made by the Out-Patient Surgeon who saw him, because a firm lesion projecting into the ampulla of the rectum was felt with the examining finger.

On examination he looked ill, anæmic and emaciated. There was some thickening of the cæcum palpable on abdominal examination and a firm projecting mass was felt in the ampulla of the rectum which appeared to encircle the lumen. This was confirmed on sigmoidoscopy. The surface was ulcerated. No other lesions were seen. Biopsy showed a chronic inflammatory lesion with areas of necrosis. At one point a small collection of cells was seen one or two of which contained red cells. These were probably *Entamœba histolytica*. Only after a provocative dose of emetine was the amœba demonstrated in the stools.

He made a complete recovery on anti-amœbic drugs.

*Confusion with an appendix mass.*—Cases which present with an inflammatory mass in the right iliac fossa and are treated by the Ochsner-Sherren method can be divided clinically into two types: (1) those which resolve readily, as the ordinary "appendix mass" will do, and (2) those which fail to improve and rather tend to linger and eventually may be shown to clear up when treated with emetine. For completeness, perhaps, the more chronic inflammatory masses in the right iliac fossa such as tuberculosis should be mentioned. Those cases which go on to frank abscess formation require drainage in either case.

*Diagnosis.*—Desjardins has made the remark that experience in diagnosis of amœbiasis determines the difference between surgical resection or medical treatment.

Individuals with chronic or latent amœbiasis will be generally below par, will usually have a secondary anæmia and appear to be in chronic ill-health.

Some authorities state that the majority of persons infected with *Entamœba histolytica* do not have dysenteric symptoms. Dysentery is, in fact, only one manifestation of the disease. Many cases present themselves with vague abdominal symptoms and give no history of dysentery at all.

Sapero (1939) states that of a series of 46 patients with non-dysenteric intestinal amœbiasis, 84.8% presented with abdominal pain and 63% had tenderness in the neighbourhood of McBurney's point.

It is clear that non-dysenteric amœbiasis presents the major diagnostic problem. A patient presenting with dysentery would certainly be suspected of amœbiasis and *Entamœba histolytica* in some form would be recognized in the stools. The absolute diagnosis does and must rest on the demonstration of the amœba.

unless the condition is kept in mind. The *entamæba* may be demonstrated in the stools or a typical lesion may be seen with the sigmoidoscope. On treatment with emetine, the granuloma usually disappears dramatically leaving very little scar tissue. The therapeutic test is therefore very helpful. The ultimate difficulty in diagnosis rests in the fact that a granuloma and a carcinoma may exist together in the same patient and at the same time.

### CASES

The following cases serve to illustrate the problems involved: Gunn and Howard reported 3 cases in 1931 in which the diagnosis of carcinoma was made; 1 was situated in the cæcum, 1 in the transverse colon and 1 in the descending colon. Resection was carried out in all the cases. They all proved to be amœbic granulomata and 2 of them died as a result of operation.

Yeomans in 1936 described a case of amœbic granuloma of the rectum and another simulating carcinoma of the colon. He emphasizes that radical treatment by surgery is almost invariably fatal unless anti-amœbic treatment has been given.

Cameron and Collins in 1942 reported a case of a corporal aged 27 who presented with acute intestinal obstruction and had one tumour in the rectum and one in the transverse colon. The condition was not suspected of being amœbic. A cæcostomy was performed, which relieved the obstruction, but a fungating mass appeared at the opening. Emetine was then given empirically and all the lesions cleared up dramatically.

Lindskog and Walters in 1946 described a case of a patient aged 27, who had had an acute attack of amœbic dysentery in September 1944. In April 1945 a recurrence failed to respond to treatment and the patient had a tumour on the right side with increasing anæmia. A right hemicolectomy was performed after previous anti-amœbic treatment and the patient made an uninterrupted recovery. The specimen showed a chronic granuloma of the ileocæcal junction with small superficial ulcers of the ascending colon. Amœbæ were demonstrated in the specimens.

My personal cases are four in number.

I.—J. H. G., aged 23.

1.9.42: Admitted to hospital in Iraq.

*History.*—Abroad five months—Capetown, Bombay, Iraq. While on board ship off Capetown in April 1942, was awakened with severe pain across the lower abdomen which radiated to the right loin and settled there. He had no diarrhoea and his symptoms settled completely in twenty-four hours. Two days before admission, pain recurred across the lower abdomen.

*State on admission.*—Temperature, pulse and respiration normal. Indefinite thickening and tenderness in the right iliac fossa. Blood and mucus present in stools. Stools negative for amœbæ and dysenteric bacilli. Mass in right iliac fossa became more definite, blood and mucus ceased. Repeated examination of stools normal.

|                    |        |         |
|--------------------|--------|---------|
| White cell counts: | 3.9.42 | 18.9.42 |
| W.B.C.             | 20,000 | 18,800  |
| Polys.             | 71%    | 79%     |
| Small lymphos.     | 20%    | 17%     |
| Large monos.       | 9%     | 3%      |
| Eosinos.           | 0%     | 1%      |

29.9.42: Complained of pain in back—ran intermittent fever. T. 100–102° F., P. 110, R. 20. Mass still present.

9.10.42: Condition deteriorating. Massive hæmorrhage.

12.10.42: Sigmoidoscopy: Granuloma present at 8 in. Typical diamond-shaped ulcers seen with ragged edges. *Entameba histolytica* demonstrated in scrapings. Course of emetine commenced. Blood transfusion (1 pint) given.

15.10.42: Much improved.

30.10.42: Sigmoidoscopy: Granuloma almost disappeared.

10.11.42: Developed typical acute attack of small bowel obstruction.

be confined to the cæcal region or some other part of the large bowel, whereas chronic ulcerative colitis is more diffuse in its distribution. Two recent studies of this subject are of some value.

Druckmann and Schorr (1945) of the Hadassah University in Jerusalem divide the manifestations of amœbiasis in the large intestine into two types: One, the diffuse type, which is not characteristic on X-ray examination and resembles idiopathic or ulcerative colitis. Two, the localized type, which presents a more characteristic picture. These lesions occur, in order of frequency, in the cæcum, ascending colon, sigmoid colon and rectum. They notice the following radiographic differences between these lesions and carcinoma: (1) The filling defect is relatively long in its extent. (2) The lesions are often multiple. Carcinomata may be multiple but very rarely so. (3) The incompleteness of the narrowing as compared with malignant stenosis. Acute intestinal obstruction is rare. (4) The pain which is so typically produced by distension of the stricture by barium in carcinoma is much less or even absent in this condition. The stricture is less rigid. (5) Frequently the abnormal area merges very gradually into the normal in this condition. (6) The elasticity of the intestinal wall remains in part and distension of the lumen can be demonstrated on the introduction of barium. (7) The mucosa relief of the involved portion of the bowel is more or less normal. This emphasizes again the fact that the submucosa is the tissue essentially affected in this condition. (8) The therapeutic test—more or less complete restoration to normal after appropriate specific treatment.

Golden and Ducharme (1945) of Columbia University, New York, studied the clinical significance of deformity of the cæcum in amœbiasis and found that a barium meal gave a more helpful picture than barium enema.

A group of 119 cases of proved or suspected amœbiasis were studied. 107 had *Entamoeba histolytica* in their stools. 67 of the 119 had a barium examination and there was a cæcal deformity in 30 cases. 21 of these 30 cases had proved amœbiasis and the disease was not disproved in the other 9 cases. Of the 58 patients who had amœbæ in the stools and who had a barium examination, 21 (i.e. 36%) had a deformity of the cæcum; 33 (i.e. 57%) had no deformity; 4 (i.e. 7%) had deformities distal to the cæcum. The deformity observed was a shortening and narrowing of the cæcum and a patency of the ileo-cæcal valve. Golden and Ducharme point out that the differential diagnosis from tuberculosis is that in the latter the terminal ileum is usually involved. It is stated that only in 5% of cases of tuberculosis of the cæcum is there no ileal involvement. Regional enteritis most commonly affects the ileum only. Carcinoma produces an irregular and asymmetrical filling defect with a palpable mass.

If all other methods of diagnosis have proved uncertain, that is, if one has failed to demonstrate the amœba by any means and one still suspects amœbiasis, the therapeutic test should be applied. A course of emetine is given and its effect is observed. As already mentioned, this may give absolute proof by producing the amœba in the stool or if the symptoms and signs are relieved, the circumstantial evidence may be very strong. The chief point in this most important differential diagnosis is that the possibility of an amœbic granuloma should be kept in mind even in people who have not lived in the so-called endemic areas.

*Treatment.*—The treatment is medical with the appropriate anti-amœbic drugs. If this has failed in a suspected case, resection may be undertaken, with the giving of further anti-amœbic drugs. This procedure will act as a safeguard in those rare cases where carcinoma and amœbic granuloma co-exist and those, equally rare, in which an amœbic granuloma does not disappear completely and readily with anti-amœbic drugs.

In those cases which present with vague abdominal pain or with definite symptoms and signs localized to the right lower quadrant of the abdomen, a saline purge will frequently cause cysts of the amœba to appear in the stools. A provocative dose of emetine may do the same. These two methods have come to be used because clinical observation has shown that a latent amœbiasis has frequently been brought to light by an attack of enteritis or bacillary dysentery *and also*, if frequent examinations of the stools are made in patients who are receiving a course of emetine as a therapeutic test, the amœba is quite commonly demonstrated.

*Sigmoidoscopy.*—In about one-third of all cases of amœbiasis there are demonstrable lesions in the rectum or lower sigmoid colon which can be seen with a sigmoidoscope. Four main types of lesion may be recognized:

(a) The frank large ulcer which may be diamond-shaped and may be single or multiple and if single or few usually show a fairly normal mucosa apart from the actual lesions. These ulcers have a raised and ragged margin with overhanging edges and a slough is visible in the floor. Usually the amœba will have been demonstrated in the stools of these cases without any difficulty, but if not a specimen of the slough from the floor of one of the ulcers should be examined.

(b) The pin-point lesion, which is so often seen on one of the valves of Houston and which consists of a raised red area with a greyish-white centre. These are often few in number and may be missed unless carefully looked for. Their centres should be scraped with a sharp instrument and examined for the amœba. Often in these cases the stool examination will have been negative.

(c) "Crateriform pits" (Cropper, 1945) are recognizable in old and quiescent cases of amœbiasis, though the non-activity may only be local. There may be active lesions higher up in the bowel. They consist of small circular depressions about 2 mm. in diameter, whose edges are raised up from the surrounding mucosa. It is not usually possible to demonstrate the amœba in scrapings from these.

(d) The amœbic granuloma, which usually has an ulcerated surface, and is easily confused with a carcinoma. In the cases that I have seen, they have been less friable than a carcinoma. A biopsy and a smear should be taken. The method of collection and examination of the specimens for amœbæ taken at sigmoidoscopy is important. A small sharp spoon with a suitably long handle to be introduced into the sigmoidoscope is the best instrument to collect the specimen, which should consist of the actual slough or secretions from the floor of the ulcer. This should be put directly upon a warmed microscope slide and mixed with a little warm saline and a cover-slip should be placed in position and the slide examined as soon as possible. In clinics abroad it was a great advantage to have a pathologist in attendance in the sigmoidoscopy room when one was doing a number of examinations.

The value of the white cell count in diagnosis is not really very great. A leucocytosis of 10,000 to 20,000 is usual with about 70% polymorphonuclear cells. There may be a slight increase in eosinophils but this is not a constant finding. The degree of leucocytosis will vary with the extent of any secondary infection that may be present.

*The value of radiology in diagnosis.*—The accepted and standard textbooks both in this country and America agree that there are no radiographic changes which make an accurate differential diagnosis of amœbiasis possible. They point out that the diagnosis rests securely on the demonstration of the entamœba, but that radiographic examination serves to indicate the degree and distribution of pathological changes. The actual findings on barium enema and on barium meal in cæcal lesions are those of any chronic inflammatory lesion which has progressed to cause some narrowing and deformity of the gut. The only fundamental distinction between amœbiasis and chronic ulcerative colitis is the tendency in the former for the lesions to

## Section of Radiology

President—J. S. FULTON, C.B.E., T.D., M.D., F.R.C.P.Ed., F.F.R.

[May 20, 1949]

### Carcinoma of the Lung

#### PRESIDENT'S ADDRESS

By J. S. FULTON, C.B.E., T.D., M.D., F.R.C.P.Ed., F.F.R.

I HAVE chosen Carcinoma of the Lung as the subject of this Address for three reasons. First, it is a disease which is of interest both to the diagnostic radiologist and to the radio-therapist. Secondly, it is a condition which appears to be on the increase, and thirdly, the suggestion has been advanced from certain quarters that the incidence of this disease is greater in the Liverpool Region than elsewhere in the United Kingdom. It occurred to me, therefore, that it might be of interest to review the cases of carcinoma of the lung which had been recorded in the Liverpool Region during the last five years, in the hope that some further light might be shed on this rather distressing problem.

The material available for study consists of 1,610 cases of carcinoma of the lung recorded in the Clinical and Pathological Register of the Liverpool Cancer Control Organization, during the five-year period 1944–1948. These figures do not include cases registered as tumours of the mediastinum as distinct from those considered to be of bronchogenic origin.

TABLE I  
*Cases Registered in Liverpool Region  
1944–1948*

|      |    |    |    |    |       |
|------|----|----|----|----|-------|
| 1944 | .. | .. | .. | .. | 210   |
| 1945 | .. | .. | .. | .. | 245   |
| 1946 | .. | .. | .. | .. | 321   |
| 1947 | .. | .. | .. | .. | 378   |
| 1948 | .. | .. | .. | .. | 456   |
|      |    |    |    |    | 1,610 |

#### INCIDENCE

It will be noted that there is an apparent and rather alarming increase in the number of cases recorded in the later years. In considering these figures, however, it is necessary to take cognizance of two factors in order to get the picture in its true perspective. First, the population served by the Liverpool Centre has extended materially since 1944, and, secondly, an increasingly live interest has been shown by participating hospitals in recording with the Registry all cases of malignant disease. It is possible to make a fairly accurate estimate of the population served each year, however, and during the period under review this discloses the following picture:

TABLE II  
*Incidence*

| Year | Population served | Cases registered | Registrations per million |
|------|-------------------|------------------|---------------------------|
| 1944 | 1,440,000         | 210              | 145                       |
| 1945 | 1,500,000         | 245              | 163                       |
| 1946 | 1,630,000         | 321              | 197                       |
| 1947 | 1,900,000         | 378              | 199                       |
| 1948 | 2,200,000         | 456              | 207                       |

Making allowance for the factor of growing interest, and increasing collaboration, it would appear that the incidence of carcinoma of the lung in the Liverpool Region is in

## REFERENCES

- CAMERON, J. A. M., and COLLINS, J. C. (1942) *J.R. Army med. Cps.*, 79, 140.  
CROPPER, C. F. J. (1945) *Lancet* (ii), 460.  
DRUCKMANN, A., and SCHOOR, S. (1945) *Amer. J. Roentgenol.*, 54, 145.  
GOLDEN, R., and DUCHARME, P. (1945) *Radiology*, 45, 565.  
GUNN, H., and HOWARD, N. J. (1931) *J. Amer. med. Ass.*, 97, 166.  
LINDSKOG, G. E., and WALTERS, W. (1946) *J. Amer. med. Ass.*, 131, 92.  
SAPERO, J. J. (1939) *Amer. J. trop. Med.*, 19, 497.  
YEOMANS, F. C. (1936) *Amer. J. Surg.*, 31, 365.

Dr. H. W. A. Post said that from the radiological appearances alone it was extremely difficult and frequently impossible to differentiate between a localized amœbic granulomatous condition and a neoplasm; in many cases where no help was obtained from the examination of the stools it would be advisable to carry out a course of anti-amœbic therapy and then to repeat the X-ray examination to assess any change that might have occurred.

A radiological examination of the character of the mucosal pattern neighbouring to and within the affected area might, however, be of great help; in neoplastic lesions the mucosal folds were usually broken, irregular in width and greatly distorted, whereas in amœbic lesions they tended to be swollen in the more active phase of the disease and flattened and narrowed in the chronic state; these folds, however, remained intact and did not show the break in their contour or the gross irregularity seen in neoplastic disease.

One other useful sign in the differentiation of the two lesions, which unfortunately was not commonly seen, was the appearance of the barium emulsion in the region of the affected area; in neoplastic disease the density of the barium emulsion remained the same as that in the rest of the colon, whereas in amœbiasis the emulsion in contact with the diseased area became more translucent owing to the outpouring of fluid by the bowel wall.



TABLE V  
Age Incidence

|         |       | Percentage<br>of total |
|---------|-------|------------------------|
| 20-29   | 16    | 1.0%                   |
| 30-39   | 91    | 5.6%                   |
| 40-49   | 332   | 20.6%                  |
| 50-59   | 570   | 35.4%                  |
| 60-69   | 463   | 28.8%                  |
| 70-79   | 127   | 7.9%                   |
| Over 80 | 11    | 0.7%                   |
|         | 1,610 |                        |

## AGE INCIDENCE

Carcinoma of the lung is a disease of later life. No case in this series was recorded below the age of 20, and the maximum incidence was recorded in the sixth decade of life.

TABLE VI  
Sex Incidence

| Year | Male  | Female | Total | Ratio   |
|------|-------|--------|-------|---------|
| 1944 | 180   | 30     | 210   | 6.0 : 1 |
| 1945 | 209   | 36     | 245   | 5.8 : 1 |
| 1946 | 283   | 38     | 321   | 7.4 : 1 |
| 1947 | 341   | 37     | 378   | 9.2 : 1 |
| 1948 | 403   | 53     | 456   | 7.6 : 1 |
|      | 1,416 | 194    | 1,610 |         |
|      | Male  | Female |       |         |
|      | 7.3   | 1      |       |         |

## SEX INCIDENCE

It has long been known that the incidence of carcinoma of the lung is higher in the male than in the female, and various figures have been published on this score. From a study of this particular series, it would appear that the disease is anything from six to nine times as common in men as it is in women. The overall picture of the 1,610 cases shows a sex ratio of 7.3 : 1.

TABLE VII  
Occupations

|                                    |    |    |     |                       |       |
|------------------------------------|----|----|-----|-----------------------|-------|
| Indoor occupations (Domestic, &c.) | .. | .. | ..  | ..                    | 456   |
| Including: Housewives              | .. | .. | 147 |                       |       |
| Clerks                             | .. | .. | 90  |                       |       |
| Small business                     | .. | .. | 47  |                       |       |
| Outdoor                            | .. | .. | ..  | ..                    | 469   |
| Including: Labourers               | .. | .. | 192 |                       |       |
| Transport                          | .. | .. | 109 |                       |       |
| Seafaring                          | .. | .. | 32  |                       |       |
| Agriculture                        | .. | .. | 18  |                       |       |
| Professional                       | .. | .. | ..  | ..                    | 84    |
| Including: Civil Service           | .. | .. | 18  |                       |       |
| Bankers                            | .. | .. | 13  |                       |       |
| Doctors                            | .. | .. | 13  |                       |       |
| Textile workers                    | .. | .. | ..  | ..                    | 19    |
| Chemicals                          | .. | .. | ..  | ..                    | 48    |
| Including: Painters                | .. | .. | 27  | (1.7% of total cases) |       |
| Metals                             | .. | .. | ..  | ..                    | 70    |
| Including: Furnacemen              | .. | .. | 30  | (1.9% of total cases) |       |
| Wood, glass, &c.                   | .. | .. | ..  | ..                    | 56    |
| Miners                             | .. | .. | ..  | ..                    | 17    |
| Miscellaneous                      | .. | .. | ..  | ..                    | 391   |
|                                    |    |    |     |                       | 1,610 |

## OCCUPATION

Information regarding occupation is given in Table VII. There appears to be little difference between the risk run by those employed in indoor as compared with outdoor occupations. In the latter group, labourers and transport workers provide the largest numbers

excess of 200 new cases per year per million of population: a figure which has remained fairly constant over the last three years under review. This means that in this region carcinoma of the lung represents one-tenth of all new cases of cancer; a truly formidable figure.

#### GEOGRAPHICAL DISTRIBUTION

The geographical distribution of the cases is given in Table III, and it will be seen that the majority of the cases appear to have occurred within the City boundaries of Liverpool. The picture is once more distorted by the administrative arrangements whereby Southport became an active participant in the scheme during the last year, and the participation of the

TABLE III  
*Geographical Distribution*

|                  | 1944 | 1945 | 1946 | 1947 | 1948 |
|------------------|------|------|------|------|------|
| Other regions .. | 13   | 8    | 4    | 2    | 6    |
| Lancashire ..    | 25   | 33   | 40   | 59   | 70   |
| Cheshire ..      | 11   | 9    | 22   | 32   | 34   |
| Isle of Man ..   | 1    | 2    | 1    | 4    | 4    |
| Liverpool ..     | 125  | 137  | 174  | 180  | 226  |
| Birkenhead ..    | 10   | 3    | 26   | 24   | 22   |
| Bootle ..        | 12   | 19   | 6    | 13   | 21   |
| Wallasey ..      | 2    | 13   | 10   | 22   | 19   |
| Southport ..     | 1    | 4    | 3    | 6    | 20   |
| Warrington ..    | 1    | 1    | 3    | 2    | 11   |
| Chester ..       | 1    | —    | 5    | 10   | 4    |
| St. Helens ..    | 4    | 4    | 14   | 7    | 3    |

rural portions of Lancashire and Cheshire took place in the year 1947. During the year 1948, however, all the County Boroughs were formally participating in the scheme, and the figures relating to this year, therefore, probably give the most accurate picture of the geographical distribution. If these figures are considered along with the appropriate population statistics, it might be possible to formulate an opinion regarding the suggested difference in the incidence of the disease in urban and rural areas. An analysis on this basis is given in Table IV.

TABLE IV  
*Regional Incidence*

|                | Cases registered<br>in 1948 | Rate per<br>100,000 |
|----------------|-----------------------------|---------------------|
| Lancashire ..  | 70                          | 27                  |
| Cheshire ..    | 34                          | 19                  |
| Isle of Man .. | 4                           | 8                   |
| North Wales .. | 10                          | 3                   |
| Liverpool ..   | 226                         | 27                  |
| Birkenhead ..  | 22                          | 15                  |
| Bootle ..      | 21                          | 28                  |
| Wallasey ..    | 19                          | 20                  |
| Southport ..   | 20                          | 25                  |
| Warrington ..  | 11                          | 14                  |
| Chester ..     | 4                           | 10                  |
| St. Helens ..  | 3                           | 3                   |

This appears to disclose a relatively high incidence in Liverpool, Bootle, and Lancashire generally, in comparison with Chester, North Wales, and the Isle of Man. The comparatively low figures for Warrington and St. Helens may, to some extent, be discounted since they were the last to join the scheme, and it is probable that all cases from these areas have not been recorded. It is of interest to note that in areas such as Birkenhead and Wallasey, which are partly industrial and partly residential, the incidence appears to occur at an intermediate level between, for example, the essentially industrial area of Bootle on the one hand, and the Isle of Man, as representing a rural area on the other. These two areas make an excellent basis for comparison since I am confident that a very high percentage of cases which occur in these two zones are, in fact, recorded in the Clinical and Pathological Register. These figures then give general support to the view that the incidence of carcinoma of the lung is higher in industrial areas than it is in rural zones.

TABLE V  
Age Incidence

|         |       | Percentage<br>of total |
|---------|-------|------------------------|
| 20-29   | 16    | 1.0%                   |
| 30-39   | 91    | 5.6%                   |
| 40-49   | 332   | 20.6%                  |
| 50-59   | 570   | 35.4%                  |
| 60-69   | 463   | 28.8%                  |
| 70-79   | 127   | 7.9%                   |
| Over 80 | 11    | 0.7%                   |
|         | 1,610 |                        |

## AGE INCIDENCE

Carcinoma of the lung is a disease of later life. No case in this series was recorded below the age of 20, and the maximum incidence was recorded in the sixth decade of life.

TABLE VI  
Sex Incidence

| Year | Male  | Female | Total | Ratio   |
|------|-------|--------|-------|---------|
| 1944 | 180   | 30     | 210   | 6.0 : 1 |
| 1945 | 209   | 36     | 245   | 5.8 : 1 |
| 1946 | 283   | 38     | 321   | 7.4 : 1 |
| 1947 | 341   | 37     | 378   | 9.2 : 1 |
| 1948 | 403   | 53     | 456   | 7.6 : 1 |
|      | 1,416 | 194    | 1,610 |         |
|      | Male  | Female |       |         |
|      | 7.3   | 1      |       |         |

## SEX INCIDENCE

It has long been known that the incidence of carcinoma of the lung is higher in the male than in the female, and various figures have been published on this score. From a study of this particular series, it would appear that the disease is anything from six to nine times as common in men as it is in women. The overall picture of the 1,610 cases shows a sex ratio of 7.3 : 1.

TABLE VII  
Occupations

|                                    |    |    |                          |       |
|------------------------------------|----|----|--------------------------|-------|
| Indoor occupations (Domestic, &c.) | .. | .. | ..                       | 456   |
| Including: Housewives              | .. | .. | 147                      |       |
| Clerks                             | .. | .. | 90                       |       |
| Small business                     | .. | .. | 47                       |       |
| Outdoor                            | .. | .. | ..                       | 469   |
| Including: Labourers               | .. | .. | 192                      |       |
| Transport                          | .. | .. | 109                      |       |
| Seafaring                          | .. | .. | 32                       |       |
| Agriculture                        | .. | .. | 18                       |       |
| Professional                       | .. | .. | ..                       | 84    |
| Including: Civil Service           | .. | .. | 18                       |       |
| Bankers                            | .. | .. | 13                       |       |
| Doctors                            | .. | .. | 13                       |       |
| Textile workers                    | .. | .. | ..                       | 19    |
| Chemicals                          | .. | .. | ..                       | 48    |
| Including: Painters                | .. | .. | 27 (1.7% of total cases) |       |
| Metals                             | .. | .. | ..                       | 70    |
| Including: Furnacemen              | .. | .. | 30 (1.9% of total cases) |       |
| Wood, glass, &c.                   | .. | .. | ..                       | 56    |
| Miners                             | .. | .. | ..                       | 17    |
| Miscellaneous                      | .. | .. | ..                       | 391   |
|                                    |    |    |                          | 1,610 |

## OCCUPATION

Information regarding occupation is given in Table VII. There appears to be little difference between the risk run by those employed in indoor as compared with outdoor occupations. In the latter group, labourers and transport workers provide the largest numbers

but these groups constitute in any case a fairly high percentage of the outdoor occupation group. Attention might be directed to the apparently high number of cases occurring among furnacemen as a small group, and also among painters. In both of these groups, possible inhalation effects must be considered. While the actual number of cases is too small to justify the drawing of conclusions, the figures point to a possible relationship and appear to warrant a more complete investigation of the incidence of the disease in these two groups.

#### TOBACCO

No attempt has been made in this group to analyse the cases in terms of the possible effect of tobacco. Case histories, unless designed in such a way as to cover this point in specific terms, do not provide information of sufficient accuracy and consistency to use as a basis for analysis. It would not be surprising to find that tobacco was an ætiological factor and, despite the fact that smoking is by no means confined to the male sex, it may have some bearing on the differing sex incidence. It may, for example, be important to determine whether the subject habitually inhales cigarette smoke, or whether it is merely puffed in the mouth. My impression is that most women smokers do not habitually inhale, while most men do.

The possible relationship between tobacco and carcinoma of the lung is being specially investigated by Dr. A. Thelwall Jones in Liverpool, and while the results of his investigation have not so far proved conclusive, the evidence to date points to tobacco as an ætiological factor of possible statistical significance.

TABLE VIII  
*Side of Chest Involved*  
Right side                      Left side

|      |           |           |
|------|-----------|-----------|
| 1944 | 107       | 79        |
| 1945 | 95        | 86        |
| 1946 | 124       | 109       |
| 1947 | 175       | 163       |
| 1948 | 191       | 179       |
|      | <hr/> 692 | <hr/> 616 |

#### SIDE OF CHEST INVOLVED

There appears to be a slightly increased incidence of the disease in the right side of the chest in comparison with the left. This slight preponderance has occurred consistently in each year under review. The pathological significance of this is not clear; it may be related to the greater surface area of the right bronchial branches and might thus lend weight to the inhalation hypothesis. Its occurrence is sufficiently regular, however, to warrant attention being directed to this feature.

TABLE IX  
*Portion of Lung Involved*

|                 |    |    |    |             |
|-----------------|----|----|----|-------------|
| Apex (Pancoast) | .. | .. | .. | 34          |
| Lung parenchyma | .. | .. | .. | 17          |
| Trachea         | .. | .. | .. | 2           |
| Main bronchus   | .. | .. | .. | 436         |
| Upper lobe      | .. | .. | .. | 421         |
| Middle lobe     | .. | .. | .. | 57          |
| Lower lobe      | .. | .. | .. | 327         |
| Indeterminate   | .. | .. | .. | 316         |
|                 |    |    |    | <hr/> 1,610 |

#### PORTION OF LUNG INVOLVED

Analysis in terms of the portion of lung involved shows that the disease tends to affect the upper lobe more frequently than the lower lobe. In the series examined, in two cases only did the disease originate in the trachea, and in 316 cases the condition was so advanced when the patient sought advice that accurate determination of the site of origin was not possible.

TABLE X  
*Duration of Symptoms*

|               |    |    |    |    |       |
|---------------|----|----|----|----|-------|
| Over 2 years  | .. | .. | .. | .. | 159   |
| 1-2 years     | .. | .. | .. | .. | 156   |
| 9-12 months   | .. | .. | .. | .. | 165   |
| 8 months      | .. | .. | .. | .. | 54    |
| 7 months      | .. | .. | .. | .. | 46    |
| 6 months      | .. | .. | .. | .. | 147   |
| 5 months      | .. | .. | .. | .. | 80    |
| 4 months      | .. | .. | .. | .. | 125   |
| 3 months      | .. | .. | .. | .. | 256   |
| 2 months      | .. | .. | .. | .. | 233   |
| 1 month ..    | .. | .. | .. | .. | 119   |
| Under 1 month | .. | .. | .. | .. | 70    |
|               |    |    |    |    | 1,610 |

#### DURATION OF SYMPTOMS

In a high percentage of cases, it is difficult in this condition to obtain accurate statements regarding the duration of symptoms. The disease is frequently superimposed on old-standing chest trouble and the patient is unable to point clearly to the time of onset of significant symptoms. The apparent discrepancy noted at the six-month period is probably not of significance, and represents the natural tendency to accept a round figure rather than a more specific time interval of five or seven months. The analysis of the history given in the 1,610 cases points to the probable mean duration of symptoms as being between two and three months.

#### CLINICAL STAGING

Four clinical stages of this disease are recognized, and details of these are as follows: (1) Localized lesion with no evidence of collapse of lung. General condition good. (2) As (1), but with visible evidence of tumour, or with early evidence of collapse, e.g. one lobe. General condition good. (3) Collapse involving whole lung on one side. (4) Extensive lesion with: (a) Pleural effusion, (b) supra-clavicular glands, (c) mediastinal glands, (d) distant metastases.

TABLE XI  
*Stage of Disease*

|           |       | Percentage<br>of total |
|-----------|-------|------------------------|
| Stage I   | 40    | 2.4                    |
| Stage II  | 159   | 10.0                   |
| Stage III | 284   | 17.6                   |
| Stage IV  | 1,127 | 70.0                   |
| 1,610     |       |                        |

Details of the staging of the cases under review are given in Table XI, from which it will be noted that no less than 70% of the patients were in Stage IV when they were first seen. In only 12.4% was the disease in a stage when radical treatment, either surgical or radio-therapeutic, might hope to meet with success.

TABLE XII  
*Absolute Survivals of All Cases Recorded*

|                              |     |       |
|------------------------------|-----|-------|
| Died of intercurrent disease | ..  | 14    |
| Died of malignancy .. ..     | ..  | 1,378 |
| Treated .. ..                | 463 |       |
| Untreated .. ..              | 915 |       |
| Remaining alive .. ..        | ..  | 218   |
|                              |     | 1,610 |

#### ABSOLUTE SURVIVALS

The present position regarding the 1,610 cases under review is shown in Table XII. From this it will be seen that 14 cases died of intercurrent disease, while 1,378 cases died of malignancy. Of these, 463 had received treatment in some form or other, while 915 had received no active treatment. There remain alive at the present moment only 218 of these patients. Leaving these cases for the moment, let us consider the incidence of metastases among those who have died.

## METASTASES

Of the total number of 1,392 patients who have died, metastases were recorded as absent in 246; information regarding metastases was indefinite in 402. while metastases were recorded as being present at death in 744 cases. Of these, details of the sites of metastases were available in 575 cases.

## SITE OF METASTASES

Details of the occurrence of metastases in these 575 cases are given in Table XIII, which is

TABLE XIII  
*Sites of Metastases*

|                             |     |
|-----------------------------|-----|
| Total number of cases .. .. | 575 |
| Metastases recorded in:     |     |
| Ovary and suprarenal .. ..  | 53  |
| Peritoneum .. ..            | 38  |
| Liver .. ..                 | 138 |
| Pleura .. ..                | 42  |
| Lung fields .. ..           | 51  |
| Brain .. ..                 | 90  |
| Bone .. ..                  | 109 |
| Glands .. ..                | 309 |
| Skin .. ..                  | 39  |

compiled in such a way that a record has been made of all metastatic deposits noted, whether isolated or multiple.

TABLE XIV  
*Cases Alive*

| Year | Total registered | Remaining alive |
|------|------------------|-----------------|
| 1944 | 210              | 2               |
| 1945 | 245              | 4               |
| 1946 | 321              | 10              |
| 1947 | 378              | 29              |
| 1948 | 456              | 173             |
|      |                  | 218             |

Turning now to the 218 cases remaining alive, we find that of the 210 cases registered in 1944, 2 only have survived. Both these patients were treated radically by X-rays. Of the 245 cases registered in 1945, 4 remain alive, 2 of whom were treated by surgery and 2 by X-rays. Histological verification of the diagnosis was definite in one of the cases treated surgically, and in one of the cases treated radiologically: in the remaining 2, the histological picture was doubtful. Of the 455 cases recorded in the years 1944 and 1945, there remain alive for a period of three years or more, 6 cases only—less than 2%. It is apparent from these figures that we are confronted by a disease in which the chances of cure are very remote indeed, and that neither in surgery nor in radiotherapy do we, at this stage, possess a satisfactory method for dealing with this relentless killing disease.

What then do we achieve by treating these patients? Is treatment in fact worth while? Have we any prospect of improving treatment method? These questions must be answered.

In endeavouring to answer the first two questions, I have compared the mean total survival period from the date of onset of symptoms of the untreated cases with the mean total survival periods estimated from the date of onset of symptoms of cases treated by a number of methods. This review covers the 1,378 patients who have died, and whose ultimate survival period is therefore known. Details are given in Table XV.

TABLE XV  
*Survival from Onset of Symptoms*

|                                             | Number | Average survival (months) |
|---------------------------------------------|--------|---------------------------|
| Untreated cases .. ..                       | 915    | 7.6                       |
| Treated cases: .. ..                        | 463    |                           |
| Nitrogen mustard .. ..                      | 12     | 5.5                       |
| Palliative surgery (i.e. exploratory) .. .. | 37     | 9.4                       |
| Palliative X-ray .. ..                      | 199    | 9.0                       |
| Radical surgery .. ..                       | 25     | 11.5                      |
| Radical X-ray .. ..                         | 190    | 14.7                      |

1,378

In this series, the untreated cases survived for an average period of 7.6 months from the date of onset of symptoms. The giving of nitrogen mustard to a small group of cases did not improve this figure: on the contrary, it appears to have hastened the end. Palliative measures apparently lengthen the span of life to a slight extent. The group of 37 patients shown as receiving palliative surgery comprise those cases in which the clinical picture was such as to warrant the chest being opened in the hope of being able to proceed to radical surgical removal, but in which this procedure at operation was found to be impracticable. They, therefore, comprise a group of comparatively early cases, and this fact must be borne in mind in assessing the significance of the period of their ultimate survival and, in particular, in attempting to compare them with the group treated by palliative X-ray therapy in all of whom the disease was in a much more advanced stage.

There appears to be a significant extension of the overall survival period if radical treatment, either by surgery or radiotherapy, is possible, and, in suitable cases, these measures would appear to be fully justified.

But the value of treatment by radiotherapy cannot be measured solely in terms of a limited extension of the survival period. The very real value of this method of treatment lies in the definite relief which it provides in relation to the distressing symptoms of pain and dyspnoea. I have no hesitation in advancing the view that the physical and, following this, the psychological benefit which accrues from treatment, even if carried to palliative dosage level only, is well worth while. In the untreated case, there is steady and progressive deterioration in the clinical picture, whereas in the treated case the patient is given a period of relief from pain and dyspnoea which may last for a year or more, the end coming suddenly and being ushered in by a short sharp illness extending over a period measured in weeks or even days. The average quality of life which remains to the patient in these circumstances is without doubt higher than if he remains untreated.

Clearly, we must keep before us the fundamental conception that we are dealing with patients as distinct from cases of a disease. The overriding principle that the cure must not be worse than the disease should be constantly before us in determining the line of treatment to be adopted with each particular patient. Radical dosage involving a prolonged and trying ordeal of treatment should not be undertaken unless there is a reasonable prospect of the patient being able to stand the treatment and benefit in consequence. As a general rule, radical treatment is attempted in Stages I and II, but clearly each case must be judged on its own merits. As a general guide, an attempt has been made to outline certain conditions which might be considered as contra-indications to treatment. Details of these are as follows:

#### CONTRA-INDICATIONS FOR RADICAL TREATMENT OF PRIMARY

- (1) Poor general condition (age, concurrent disease, &c.).
- (2) Pleural effusion.
- (3) Any clinically or radiologically demonstrable extension beyond primary site, e.g. radiologically visible mediastinal glands or extrathoracic metastasis.
- (4) Collapse involving lobes of both sides.

#### CONTRA-INDICATIONS FOR PALLIATIVE TREATMENT OF PRIMARY

- (1) Poor general condition.
- (2) Distant metastases other than supraclavicular glands.
- (3) Evidence of breaking down of primary, e.g. lung abscess.
- (4) Pulmonary tuberculosis likely to be activated by treatment.

#### INDICATIONS FOR PALLIATIVE TREATMENT OF LESIONS OTHER THAN THE PRIMARY

Extensions of primary or metastases producing symptoms which may be relieved by radiotherapy,  
e.g. Pain,

Mediastinal obstruction,

Isolated bone metastases causing pain,

Cerebral metastases with localizing symptoms.

It would, I think, be fair to say that our methods are improving. Surgical techniques have advanced and, with growing experience, a more accurate clinical evaluation of cases suitable for surgery is being made. The closest collaboration between the thoracic surgeon and the radiotherapist is essential in this field. Those of us who come in contact with a large number of cases of cancer will readily subscribe to the view that, as a life-saving measure, radical

## METASTASES

Of the total number of 1,392 patients who have died, metastases were recorded as absent in 246; information regarding metastases was indefinite in 402 while metastases were recorded as being present at death in 744 cases. Of these, details of the sites of metastases were available in 575 cases.

## SITE OF METASTASES

Details of the occurrence of metastases in these 575 cases are given in Table XIII, which is

TABLE XIII  
*Sites of Metastases*

|                             |     |
|-----------------------------|-----|
| Total number of cases .. .. | 575 |
| Metastases recorded in:     |     |
| Ovary and suprarenal .. ..  | 53  |
| Peritoneum .. ..            | 38  |
| Liver .. ..                 | 138 |
| Pleura .. ..                | 42  |
| Lung fields .. ..           | 51  |
| Brain .. ..                 | 90  |
| Bone .. ..                  | 109 |
| Glands .. ..                | 309 |
| Skin .. ..                  | 39  |

compiled in such a way that a record has been made of all metastatic deposits noted, whether isolated or multiple.

TABLE XIV  
*Cases Alive*

| Year | Total registered | Remaining alive |
|------|------------------|-----------------|
| 1944 | 210              | 2               |
| 1945 | 245              | 4               |
| 1946 | 321              | 10              |
| 1947 | 378              | 29              |
| 1948 | 456              | 173             |
|      |                  | <hr/> 218       |

Turning now to the 218 cases remaining alive, we find that of the 210 cases registered in 1944, 2 only have survived. Both these patients were treated radically by X-rays. Of the 245 cases registered in 1945, 4 remain alive, 2 of whom were treated by surgery and 2 by X-rays. Histological verification of the diagnosis was definite in one of the cases treated surgically, and in one of the cases treated radiologically: in the remaining 2, the histological picture was doubtful. Of the 455 cases recorded in the years 1944 and 1945, there remain alive for a period of three years or more, 6 cases only—less than 2%. It is apparent from these figures that we are confronted by a disease in which the chances of cure are very remote indeed, and that neither in surgery nor in radiotherapy do we, at this stage, possess a satisfactory method for dealing with this relentless killing disease.

What then do we achieve by treating these patients? Is treatment in fact worth while? Have we any prospect of improving treatment method? These questions must be answered.

In endeavouring to answer the first two questions, I have compared the mean total survival period from the date of onset of symptoms of the untreated cases with the mean total survival periods estimated from the date of onset of symptoms of cases treated by a number of methods. This review covers the 1,378 patients who have died, and whose ultimate survival period is therefore known. Details are given in Table XV.

TABLE XV  
*Survival from Onset of Symptoms*

|                                          | Number      | Average survival (months) |
|------------------------------------------|-------------|---------------------------|
| Untreated cases .. ..                    | 915         | 7.6                       |
| Treated cases: .. ..                     | 463         |                           |
| Nitrogen mustard .. ..                   | 12          | 5.5                       |
| Palliative surgery (i.e. exploratory) .. | 37          | 9.4                       |
| Palliative X-ray .. ..                   | 199         | 9.0                       |
| Radical surgery .. ..                    | 25          | 11.5                      |
| Radical X-ray .. ..                      | 190         | 14.7                      |
|                                          | <hr/> 1,378 |                           |



JOINT DISCUSSION No. 2

**Section of the History of Medicine  
with Section of Odontology**

Chairman—E. ASHWORTH UNDERWOOD, M.A., M.D., D.P.H. (President of the  
Section of the History of Medicine)

[March 28, 1949]

C. E. WALLIS MEMORIAL LECTURE, 1948

[Number 4]

**The Contributions of King's College, London, to the Science of Dentistry**

By F. N. DOUBLEDAY, F.D.S., M.R.C.S.

C. E. WALLIS, the Founder of this Lecture, was educated at King's College. He became Dental Surgeon to King's College Hospital and Lecturer in the Medical School. As Principal Assistant Dental Officer he did much to establish the magnificent School Dental Service of the London County Council. During the years in which I was Editor of the *British Dental Journal*, Wallis was Chairman of the Editorial Committee and I knew him well. Quiet, courteous, having a scientific outlook on life, he established this endowment and a prize at the hospital to which he belonged.

Those whose work is to be especially recorded here are as follows:

Thomas Bell, 1836–80. Professor of Zoology at King's College.

John Tomes and S. J. A. Salter. Students of King's College.

Professors of Dental Surgery at King's College:—

Samuel Cartwright, F.R.C.S., 1860–75.

S. Hamilton Cartwright, 1875–87.

Ashley Gibbings, 1887–89.

Arthur Swayne Underwood, 1889–1911.

Lecturer on Preventive Dentistry at King's College:—

J. Sim Wallace, 1923–28.

Among the theses submitted at the University of Edinburgh, for the degree of Doctor in Medicine in 1783, is one by Thomas Bell [1], entitled “*Quædam de Diætâ seu materia diætetica*”. The author is described as *Hiberniensis*, the copy in the Library of the Royal

OCT.—JOINT. DISC.

surgical removal of a tumour, when practicable, is the method of choice. The fullest co-operation must, therefore, be extended to the thoracic surgeon in respect of those cases in which radical removal appears practicable. On the other hand, the thoracic surgeon must, so far as is possible, refrain from opening a chest when the probability of his being able to proceed to radical surgery is seriously in doubt, since, in such a case, the chances of effective treatment by radiotherapy are delayed and seriously jeopardized. We are alive to this problem in Liverpool, and are at present developing a unit in which radiotherapeutic measures may be employed through the open chest at the time of operation in those cases in which radical surgical removal proves to be impracticable.

In conclusion, I should like to take this opportunity of expressing my appreciation of the very helpful collaboration which has been extended to me by my medical and surgical colleagues in Liverpool, whose work in providing the clinical records of these patients has made this review possible. In particular, I should like to refer to the staff of the Thoracic Unit whose collaboration in this problem has been invaluable.

It is, I suppose, unusual to choose for a Presidential Address a subject in which the picture is so gloomy. My hope is that the sombre nature of this picture will constitute a challenge to you to peer into the shadows to see what lies behind: to strive constantly to solve the riddle of why this disease should be a man-killer, and why, indeed, it should occur at all. I hope that you will meet the challenge of end-result by further sustained endeavour. Our methods both surgical and radiotherapeutic are improving, and I would urge you not to accept this disease as incurable, but to continue your efforts with unabated energy.

Bell [9] co-operated with many of the leading scientific men of his day. In 1845, Sir Richard Owen [10] dedicated his great work "Odontography" to him. Odontology owes a great debt to Sir Richard Owen. Those who study his portrait, hung in the entrance hall of the Natural History Museum at South Kensington, or the amusing caricature of him which is in the Common Room in our own house, will see that he had an irascible side to his character. This sometimes came out in careless handling of certain matters. For instance, on page 472 of his first volume [he has this footnote "(1) This is the conclusion to which my friend Professor Bell has arrived in his 'Physiological Observations on the Natural Food of Man, deduced from the characters of the Teeth' on 'the Teeth, 8vo 1829, p. 33.'" It is not easy to realize that this is the title of a chapter of Bell's book "On the Anatomy and Diseases of the Teeth". A still more gross example is found on p. X of the Introduction to the "Odontography". In his dental textbook Bell gives this account of his post-mortem observations: "It is true that, as Mr. Hunter and other authors object, the teeth have never been artificially injected, but this circumstance cannot be considered as conclusive against their vascularity, for we know that many other structures contain vessels adapted only, under ordinary circumstances to the passage of the serous part of the blood; which vessels, under active inflammation, become so much enlarged as to convey the red particles also. The fact that the teeth are not generally tinged with red blood when in a state of inflammation, may be accounted for by the supposition that the bone is of so very dense a structure, as to prevent, in many cases, the slightest degree of distension of the vessels permeating its substance. I have, however, in many instances on purposely breaking a tooth immediately after extraction, where the pain and inflammation had been severe, found red patches, in the very substance of the bone. Although no artificial injection of the teeth has ever been satisfactorily made, it is unfair to deny its possibility, for the colouring matter of all the injections hitherto employed, is composed of particles too gross to pass into vessels of such extreme tenuity as those of the tooth must necessarily be; but what art has failed to effect, nature, or rather disease have [*sic*] done for us; I have in my possession a set of teeth, from the head of a young woman who died of jaundice, every one of which is deeply tinged with a bright yellow colour. I have frequently examined the teeth of persons whose death has been occasioned by hanging or drowning, and have invariably found the whole of the osseous part coloured with a dull deep red, which could not possibly have been the case if these structures were devoid of a vascular system. In both instances the enamel remains wholly free from discolouration." No one would expect Bell, writing in 1829, to know the relative diameter of the dentinal tube as compared with that of an erythrocyte but his careful attention to post-mortem examination and his deductions are worthy of high scientific praise. Owen's quotation of this passage almost verbatim and without acknowledgment is not praiseworthy.

Another great scientist, with whom Bell's work as a Professor at King's brought him into contact, was Darwin. When Darwin returned from the voyage of H.M.S. *Beagle*, he was disappointed at the lack of interest in the specimens which he had laboriously collected during the voyage but he records in a letter written in 1840: "Mr. Bell I hear is so much occupied that there is no chance of his wishing for specimens of reptiles." But a little later he says: "I became acquainted with Mr. Bell, who, to my surprise, expressed a good deal of interest about my crustacea and reptiles and seemed willing to work at them" [11]. The acquaintance evidently ripened; in 1861 Darwin mentions dining with Bell at the Linnean Club. This friendship resulted in the publication of Bell's work on Crustacea [12], and in his contribution to "The Zoology of the Voyage of H.M.S. *Beagle*". Part V of this work is written by Bell [13]. The section consists of 51 folio pages and twenty coloured plates. Usually, Bell does not describe the teeth of the specimens of Reptilia of which he gives general descriptions. In the case of the Amphibia he does give an account of the palatine teeth. For example, genus *Limnocharus*, species Bell. "The genus *Limnocharus* is remarkable for the existence of palatine teeth in a part of the mouth in which they have never before been observed in any other amphibian. Not only is there a small group or line of these contiguous with the anterior margin of the posterior nares—a situation in which they are found in some other genera of Ranidæ, but there is also a group of them placed at some distance behind the posterior margin of these openings, and close within the rise of the maxillary arch." As President of the Linnean Society, Bell occupied the chair at the famous meeting of the Linnean Society in 1858, when the original contributions of Charles Darwin and Alfred Russell Wallace were read. Bell not only occupied the chair, his firm grip of the principles involved had been shown in his observations upon retective colouring, contained in his "British Quadrupeds" (1837).

Darwin [14], in the "Origin of Species", devoted a thoughtful chapter to this subject. Alfred Russell Wallace [15], in his "Darwinism", devotes no less than three chapters to this problem. Here is what Bell [7] wrote about it in 1837. He begins by discussing at length

College of Surgeons of England is marked in pencil, "died in Dublin, Dec. 15th, 1815." Whether this man was related to our Thomas Bell I am not yet sure. Thomas Bell was born at Poole, in Dorsetshire, on October 11, 1792, the son of a surgeon who is said to have come from the north of England. He had one sister. The children were brought up by their father to an open-air life and were trained to run about barefoot in all weathers. In this beautiful Dorset country Bell acquired that love of natural history which was his chief interest throughout life. As Poole harbour was the chief station of the ships engaged in the whaling industry, this must also have brought before him another aspect of zoology. In accordance with the custom of the time, he commenced his medical education with an apprenticeship to his father, after which he entered as a student at the joint hospitals of Guy's and St. Thomas's in 1813. Among his teachers was Joseph Fox, through whose lectures [2] he became interested in dentistry. As this is the first account given before this Society of dental teaching in the London hospitals it is desirable to say that the lectures in Dental Surgery given by John Hunter [3] and published in 1771 and those by Rae [4] given in the XVIIIth century, but first published in 1858, were private courses of lectures. The first series to be officially given in a teaching school were those delivered by Joseph Fox in 1799 and published in 1803. Bell obtained his M.R.C.S. in 1815. In 1817 he was appointed as Lecturer in Comparative Anatomy at Guy's. In the same year, upon the death of Fox, he was appointed to succeed him as Surgeon Dentist to Guy's Hospital and Lecturer on the Anatomy and Diseases of the Teeth in the Medical School. These lectures [5] were published in 1829, a second edition appeared in 1835. The dental aspect of Bell's life belongs to the history of Guy's and I have told it in the history of that hospital. The account of Bell's life at King's is that of a zoologist. He founded the *Zoological Journal* in 1825; in 1827 his paper "On the Structure and Use of the Submaxillary Odoriferous Glands in the genus *Crocodylia*" [6] appeared. In 1828 he was elected a Fellow of the Royal Society, at the age of 36. His published work led to his being appointed as Professor of Zoology at King's College in 1837. This chair he held until 1882. Mr. Combridge, the Registrar of King's College, believes that this is a record for the tenure of a professorship at the College. Towards the end of this period Bell was an old man, living in the country, and undertaking no active duties. His international reputation and continued literary output seem to have been the ground on which he retained the chair<sup>1</sup>.

Bell's first published book on Zoology was "A History of British Quadrupeds" [7], which must be accounted as a popular work since it abounds in anecdotes concerning natural history. When in describing an animal he gives the dental formula he includes the teeth on both sides of the mouth thus:

$$\text{Common Otter. I. } \begin{array}{cccc} 6 & 2 & 6 & 4 \\ 6 & 2 & 6 & 4 \end{array} \begin{array}{c} \text{C.} \\ \text{F.M.} \\ \text{M.} \end{array} = \frac{18}{18}$$

He describes well the process of formation of the successional teeth in his dental textbook. This had been investigated by Blake [8], who would not publish his results until he had examined the dissections made by Fox, some of which are still in the Gordon Museum at Guy's Hospital and had no doubt been examined by Bell when he was a student there. Bell's account of the process is as follows: "The formation of the permanent teeth although essentially proceeding upon the same general principle and produced by some means of similar structures as those by which the temporary ones are formed, differs in some very remarkable points from that process, and forms, if possible, a still more beautiful and interesting illustration, both of the variety and harmony with which the different formative processes of animal organization are carried on. The rudiments of the permanent teeth, instead of being original and independent, like those of the temporary, are in fact derived from them, and remain for a considerable time attached to and intimately connected with them. At an early period in the formation of the temporary teeth, by a process which reminds us of the gemmiparous reproduction in the lower classes, both of animal and vegetable life, the investing sac gives off a small process or bud, containing a portion of the essential rudiments; namely, the pulp covered by its proper membrane. This constitutes the rudiment of the permanent tooth. It commences in a small thickening on one side of the parent sac, which gradually becomes more and more circumscribed and at length assumes a distinct form, though still connected with it by a peduncle."

<sup>1</sup>Bell's international record as given on the title page of the second edition of "A History of British Quadrupeds", published in 1874 [16], is as follows: "Member of the Philomathic and Natural History Societies of Paris; of the Imperial Academy Cæsar: Leopold: Naturæ Curiosorum; of the Hungarian Academy of Sciences; of the Academy of Sciences of Philadelphia; of the Natural History Societies of New York and Boston; Honorary Member of the Royal Zoological Society of Ireland, etc., etc.; late President of the Linnæan Society."

the inner part, near the pulp, the pulp cells had reverted to their normal function and had reformed a thin layer of tubular dentine. The first demonstration of lipoid degeneration in the dental pulp and of the translucent zone and dead tracts will be found in his papers and book.

Having spent much time, for many years, in dental research, I say, without hesitation, that in the study of the pathology of the teeth there are two outstanding landmarks, John Hunter as the earliest and Frank Colyer in our own time. Between them there is no pathologist who approaches James Salter.

Many of the teachers whose work I have to describe became teachers of the London School of Dental Surgery, later the Royal Dental Hospital. To the clinical observations of John Tomes, the work of Charles Tomes in comparative anatomy, of the scientific researches of Howard Mummary, N. G. Bennett and Frank Colyer, we all pay great homage. The authors themselves described the work here recorded as coming from King's College.

Samuel Cartwright, F.R.C.S., is stated to have been educated at Trinity College, Cambridge, and at the London Hospital, from which he obtained his M.R.C.S. in 1838.

The authorities of Trinity College, Cambridge, have most courteously investigated this question for me and send the following information regarding the entries in their books:

Cartwright, Samuel. Pensioner, April 24, 1832. Tutor, Mr. Whewell. No other particulars are given. He matriculated, 1832, but did not graduate. It is an interesting question as to whether this was Samuel Cartwright, F.R.S., the father, who practised most successfully, without any medical qualification, and may have been trying to regularize his position, or Samuel Cartwright, the son. In 1844 Samuel Cartwright, F.R.C.S., was appointed to succeed John Tomes as Dental Surgeon to King's College Hospital [20]. In 1860 he was appointed the first Professor of Dental Surgery at King's College; in 1864 he became a Member of the Board of Examiners in Dental Surgery at the Royal College of Surgeons. He was President of the Odontological Society in 1863 and again in 1877. With John Tomes and others he played a great part in the development of dental education. In consequence of this the Association of Surgeons practising Dental Surgery in 1884 founded a Prize and Medal in his honour. In 1900 this was transferred to the Royal College of Surgeons [21]. The lectures delivered by Samuel Cartwright at King's have been published [22]. There are twelve of them, comprising a total of some 7,000 words. Cartwright shows his acquaintance with a wide range of dental history. He quotes Herodotus to show that dentistry was a specialized practice in ancient Egypt, Hippocrates as using the term *σφρονισλῆρες* = wisdom tooth, and Galen as referring to *ὀφθαλμοὶ* or eye teeth. He quotes from the lectures of Ambroise Paré, Fox, Blake and Bell. He says that Guy's and St. Thomas's were the only hospitals which had previously had courses in Dental Surgery. He gives a good account of ulcerative and of gangrenous stomatitis in children, noting cases where these conditions were the sequelæ to exanthematous fevers. He also saw many cases of stomatitis and necrosis following the long-continued administration of mercury to children. In discussing the causes of the irregularity of the teeth, he makes this very just observation: "Bodily exercise and freedom of motion are conducive, indeed absolutely necessary, to the perfect development of parts." In discussing treatment by appliances he advocates capping the first permanent molars as an anchorage point. He also, like John Tomes in his lectures, describes the ribbon arch, which is so often ascribed to Edward H. Angle of St. Louis, Missouri. In fact it was described by Joseph Fox in 1799. Both these methods have the disastrous effect that they prevent the full eruption of the crown of the first permanent molar and allow the over-eruption of the lower incisors. If the reverse is done, and an upper bite plate is inserted to keep the lower incisors down and allow the first molars to erupt fully, the powerful internal pressure of the tongue will be exerted to the full extent on the inner aspect of the alveolar process and the teeth.

The credit for the introduction of tooth forceps is claimed by Cartwright on behalf of his father: "To my father is due the merit of having introduced forceps of scientific construction, he having, years gone by, materially improved those in use." There is an illustration of dental forceps in the first edition of Bell's textbook of 1829, but the earliest description appears to be that of Fay [23]. Cartwright, with his partner, Alfred Coleman [24], gave an account of the skulls in the crypt of Hythe Church. Examining about 200 maxillæ, they described the well-developed maxillary arches. The teeth were remarkable for regularity, neither having spaces between them nor being pressed together, but just touching one another laterally. In dimension the teeth appeared to differ little from those of the present day, excepting in the gradually diminishing size from the first to the third molar, which was noticeable. In a large proportion the masticating surfaces of the teeth were much worn, there was a general absence of tartar upon the surfaces of the teeth.

Alfred Coleman is known as a great teacher at the Royal Dental Hospital. When

the various views then held as to the reasons for the changes in colour of the fur or feathers of certain animals, to correspond with the changing colours of nature in summer and in winter. He recounts various experiments which have been carried out; but eventually concludes with his own opinion as follows (p. 153): "But what is the final cause of this curious phenomenon? What object, connected with the well-being of the subjects of it, does it effect in their favour? One object undoubtedly is the safety they obtain by the concealment afforded them, by an approximation to the colour of the earth's winter covering. The Ptarmigan, the Alpine hare, and many other mammalia and birds, are all more or less liable to become the prey of rapacious birds or quadrupeds, which are directed in the chase by their sight. The mottled browns which form the principal summer colours of these creatures, are well adapted for their concealment amongst the brown heaths and ferns of the summer and autumn; but such colours would render them conspicuous by contrast amongst the snows of winter."

In 1860 Bell was appointed as senior member of the first Board of Examiners for the L.D.S. In 1874 a second edition of Bell's "British Quadrupeds" appeared [16], in which Bell was assisted by Robert F. Tomes, brother of John Tomes. In 1877 Bell issued a new edition of Gilbert White's "Selborne" [17]. He bought, and for twenty years lived in, Gilbert White's house, "The Wakes", at Selborne. His own footnotes illustrate and greatly add to the wealth of knowledge contained in this delightful book. Bell's edition has the second volume containing many pictures of life among the family and friends of the original author.

In the Council Chamber of the Linnean Society, in Burlington House hangs a portrait of Bell, his bust, in marble, stands at the foot of their main staircase. A bust of Bell, presented to this Society in 1864, has now disappeared and I have not been able to discover its location.

Two King's men who were students in Bell's time attained to great distinction in later life. They were John Tomes and S. J. A. Salter.

Tomes was the son of John Tomes of Welford in Gloucestershire. He was born on March 21, 1815. In 1831 he became a pupil to Thomas Farley Smith, a surgeon of Evesham. In 1836 he entered as a student at King's. As there was no hospital attached to the College at that time, Tomes also entered at the Middlesex Hospital for clinical practice. In 1839 he obtained his M.R.C.S. and became a House-Surgeon at Middlesex during 1839-40. In 1840 he was elected Dental Surgeon to King's College Hospital, which had just been opened, and held this appointment until 1844. His later work belongs to the Middlesex and Royal Dental Hospitals: *John Tomes has honour enough in his own right.*

S. J. A. Salter was the son of a surgeon who came of a Quaker family, from Somerset, and who married the sister of Thomas Bell. Salter was born at Poole in 1825. After an apprenticeship to his father he entered King's College. By the courtesy of the present Dean, Canon Eric Abbott, and by the research of the Registrar, Mr. Combridge, I am able to publish, for the first time, the details of James Salter's very brilliant academic career. In 1846 he won a Certificate of Honour in Botany. In 1847 he won the College Prizes in Medicine and Midwifery. In 1848, in the examination for the M.B.London, he was awarded the Gold Medal in *Materia Medica and Pharmaceutical Chemistry*, and the Gold Medal in Chemistry. In 1847 he obtained his M.R.C.S. and L.S.A., and his M.B.London in 1849. He was elected an Associate of King's College in 1848 and a Fellow in 1876; for several years he was a member of the Governing Body of King's College. Salter [18] published papers of general pathological interest and originally intended to practise medicine. He was, however, appointed as Dental Surgeon to Guy's Hospital and his dental history belongs to that Foundation.

The formation of secondary dentine, as a reaction to injury, had been demonstrated by John Hunter [3], in the case of attrition, and further described by Fox [2] and by Bell. John Tomes was the first to show that it also occurred beneath advancing caries but he did not demonstrate its particular relation to the lesion; he only stated the fact in general terms. Salter [19] was the first to show, in this communication, that secondary dentine was formed exactly at the inner ends of those dentinal tubes which were undergoing surface irritation. He showed that not only does the dentine of repair correspond with the amount of injury done to each tube but that it is limited by the internal abutment of those tubes which are at the edge of the worn surface. This is an original and exact piece of observation. Another important observation was made upon a lower molar tooth, with three aberrant canals of Hesse at the neck of the tooth. Within the pulp chamber hypertrophic pulpitis (the pink spot of Howard Mummery) had occurred. The areas of absorption were beautifully shown in the section, and the outer part of this area had been filled in with osteodentine, while in

to the principal facts relating to the subject. This he does in a lucid manner, leaving upon the mind of the reader the clear impress of scientific data, agreeably stated. He showed great interest in Comparative Anatomy and founds his interest in the fact that the fossil teeth persist longer than any other parts of the body and so have especial interest in the paleontological record.

Underwood [27, 28] took part in important discussions upon the surgical anatomy of the maxillary sinus. After examining 150 skulls in the Museum of the Royal College of Surgeons, he made the following observations: Where all the cheek teeth were in position the cavity extended about half an inch to a quarter of an inch behind the third molar, which tooth is invariably in relation to its floor. The second and first molars were almost always in relation to the cavity, the second premolar generally, the first premolar fairly often, the canine rarely. He found that in normal cases the floor of the sinus was about half an inch deeper than the floor of the inferior meatus and that the deepest part was between the roots of the second molar tooth. The floor of the sinus sloped slightly upwards, anteriorly and posteriorly from this point. During the eruption of a molar, the floor of the sinus was raised in a bony dome over the crypt; this dome was absorbed and became a concave basin after eruption. The roots of the premolars were often visible as bony eminences on the floor, and, in some cases, the roots of the molar teeth also. They were rarely bare of bone and actually projecting beneath the mucous lining of the sinus. When all the teeth in relation to the sinus had been lost, the floor rose to the level, or even above, that of the nasal meatus. Where only a few teeth had been lost, the elevation of the floor was confined to that area. Of thirty-three maxillæ which had been sawn across, bony septa were observed, rising vertically about a quarter to half an inch above the floor of the sinus. Fourteen of these cases were on the left side and five on the right. The left sinus was markedly smaller than the right in eight skulls; the right never smaller than the left. Underwood did not correlate this with deviation of the nasal septum. He observed that where there was evidence of chronic abscess on the teeth, their apices had always been walled off by bony thickening, arising as a reaction to injury.

The year 1923 saw an important development in the history of King's College, the founding of the Dental School. Today the textbooks written by T. W. Widdowson are read all over the world. To the fame of its teachers and the excellence of its equipment I cannot do full justice in this paper. I do, however, want to refer to the work of J. Sim Wallace. He was the Lecturer on Preventive Dentistry on the original staff of the school, and in this capacity published two important books [29, 30], one for the education of the general public, emphasizing the value of functional mastication and of the cleansing effects of fibrous foods; the other was of a highly scientific character. In 1927, upon the Foundation commemorating another King's man, Samuel Cartwright, Wallace published lectures on "Variations in the Form of the Jaws". In his opening chapters Wallace defines the meaning of Variation. The subject of the genes of heredity as elaborated by the researches of Galton, De Vries and Mendel, has not yet been sufficiently studied in regard to the jaws. But this is a subject which lends itself well to biometric investigation. An examination of the models of two or three generations of families from a race of purer descent, such as the inhabitants of England, compared with a similar series of models of the jaws and teeth of races of mixed descent, such as those of the United States, would afford evidence of much scientific importance. In his study of variations Wallace [30] shows that the arch of the lower jaw varies, as does the upper, in relation to the body of the jaw upon which the dental arches are placed. He discusses the importance of function as shown by the effects of pressure and tension strains on the growth of the jaws. Among other examples he describes an inversion of the angle of the mandible, seen in the skulls of Esquimaux, produced by the development of the masseter muscle which results from the habit of chewing leather with their incisor teeth. Wallace attributes great importance to the muscular action of the tongue and suggests that the power so exerted is greatest during the period of development, when the jaws and dental arches are easily moulded.

In conclusion may I put this question. This account has shown dental teachers exchanging knowledge, as we do now, for the common advancement. Is it not possible, to have every year, in each of the Dental Schools of the University of London in rotation, a series of lectures recounting advances in certain fields of knowledge? Such systematic lectures have been given this term, by Professor Haldane at University College, upon Evolution, and at the Pharmaceutical Society, by Professor Paneth upon Radio-activity. At each lecture the theatre has been packed from the roof to the last space around the lecturer's desk, by great numbers of students, young and old, of many nations. There is room for such lectures in our dental schools. They arouse the imagination of students; such lectures stimulated one student to paint above his bedroom door this motto: *Hic scientia gratia est*.

the account of his work on dental caries is considered it will be found that it contains the original experiments upon the chemico-parasitic theory and that there is reason to believe that the work from which this arose was connected with King's. Robertson [25] of Birmingham had made a careful study establishing the fact that caries was a pathological condition arising on the surface of the tooth. Before his paper this had been disputed. In 1861 Coleman [26] read a paper before this Society. He says: "Following out the researches of others, I confess I was somewhat surprised, in my investigations carried out a few years ago, to find so little evidence of acid fluids in the mouths of many persons whose teeth presented the conditions of rapid decay. In the cavities themselves I found invariably an acid reaction. The acid found in the cavities of the teeth has been accounted for by the action of the decomposing tissues of these organs upon certain of the constituents of our food; but I think it is more probably due to the formation of an acid phosphate of lime, furnished by the decomposition of the lime salts of the dentine. Bone earth, exposed to warmth and moisture—conditions favourable to decomposition—undergoes a kind of putrefactive fermentation, and furnishes the same acid phosphate of lime (the superphosphate) that is produced by the action of sulphuric acid on the same substance. The conclusions I have therefore arrived at are, that certain substances generally, owing to the changes going on in the amylaceous constituents in the mouth, may by their continued contact with a tooth in the abnormal condition just spoken of, communicate a change to its particles, and induce in it disintegration or decay."

The experiments which Coleman made were as follows: From recently extracted teeth, the carious and softened portions of the dentine were carefully removed, leaving only the hard dentine exposed. Several of the teeth so prepared were put into separate flasks with the following contents:

| Flask                                      | Effect on the teeth             |
|--------------------------------------------|---------------------------------|
| 1. Roast meat finely divided and water ..  | None                            |
| 2. The same with addition of saliva ..     | None                            |
| 3. A strong solution of cane sugar ..      | Slight softening of the dentine |
| 4. The same with the addition of saliva .. | Dentine considerably softened   |
| 5. A small quantity of bread and water ..  | Slight softening                |
| 6. The same with saliva added ..           | Marked softening of the dentine |

Flasks 1 and 2 had a strongly acid alkaline reaction; flasks 3 and 4 a strongly acid reaction; flasks 5 and 6 a slightly acid reaction.

These experiments are the model for those later described by Miller. The action of the micro-organisms was not understood until the researches of Pasteur, Lister, Koch and others had shown their nature. Coleman could not be expected to recognize that what he attributed to the saliva was really due to micro-organisms within the saliva. His experimental methods and his conclusions were correct.

Mr. Frank Coleman informs me that his father and Lord Lister were connected by marriage and were on terms of close friendship. The experiments which Lister carried out on fermentation and which showed the production of lactic acid were being thought out at that time. Is it not probable that the experiments carried out by Coleman were the result of discussions with Lister?

Samuel Cartwright was followed as Professor of Dental Surgery by his son, S. Hamilton Cartwright. He was succeeded by Ashley Gibbings who only held his appointment for a short time.

Arthur Swayne Underwood was educated at King's College, where he was the Warneford Scholar in 1872. He obtained his M.R.C.S. in 1877 and completed his dental studies at the Dental Hospital of London, obtaining his L.D.S. in 1878. In 1889 he was appointed as Professor of Dental Surgery at King's College and Dental Surgeon to King's College Hospital. These appointments he continued to hold until 1911. From 1900–10 he was an Examiner in Dental Surgery at the Royal College of Surgeons and in 1911 was appointed by the General Medical Council as Inspector of Examinations. The Tomes Prize for 1906–08 was awarded to him for his work in histology. He was President of the Odontological Society in 1903–4. In 1881 he published a book "Surgery for Dental Students"; in 1887, "Aids to Dental Surgery"; in 1893, "Notes on Anæsthetics"; in 1902, "Aids to Dental Anatomy" and in 1903, "Comparative Odontology". In the Introduction to one of his books Professor Underwood says: "In all cases my object has been to interest the student in the first place and to instruct in the second, for it is my experience that once a student is interested in a subject its study is no longer a toil, but a delight, and the facts and details become as much part of his daily equipment as his hat and his umbrella." Underwood introduces the student



## Section of Neurology

President—WILLIAM JOHNSON, M.C., M.D., F.R.C.P.

[May 5, 1949]

MEETING AT THE MAIDA VALE HOSPITAL FOR NERVOUS DISEASES, LONDON, W.9

Chairman—W. RUSSELL BRAIN, D.M.

**Encephalo-Myelo-Radiculitis: A Chronic Form.**—DOUGLAS MCALPINE, M.D., F.R.C.P.,  
and FRANCIS PAGE, M.D., M.R.C.P.

J. N., aged 31. Farmer's foreman.

*History.*—September 1947: Developed double vision due to left external rectus palsy.

November 1947: Severe headache lasting for three weeks, with anorexia and occasional vomiting. He became drowsy, lethargic and apathetic.

December 1947: Gradual onset of deafness, tiredness and weakness of legs so that he tended to trip when ploughing, "pins and needles" in both lower limbs and weakness and clumsiness of both hands. Dr. R. Staley of Thetford noted mental deterioration: "From being a bright intelligent young man he became very clumsy and stupid. He would fall off to sleep for long intervals and was difficult to rouse. His speech was inarticulate and he was very deaf. There was marked weakness of arms and legs of lower motor neurone type."

January 1948: Admitted to West Suffolk Hospital as a cerebral tumour suspect. C.S.F.: Raised pressure; cells 130 per c.mm. (95% polys.); protein 100 mg. %. He was transferred to Hill End Hospital, St. Albans, under the care of Mr. J. O'Connell. On full investigation no evidence of a cerebral tumour was found. An E.E.G. showed bursts of theta waves bilaterally. Weakness of his limbs, especially of proximal muscles, was noted, with tremor on voluntary movements. No reflex or sensory changes were present. On returning home his condition further deteriorated. He had difficulty in micturition.

15.6.48: Admitted to Middlesex Hospital.

Orientated in time and space. Mental state difficult to assess on account of deafness, but some degree of deterioration evident. Sleepy by day, restless by night. No aphasia, agnosia, or apraxia. Speech dysarthric. Pallor temporal half left disc. Vision J2 both eyes. Rotatory nystagmus to right and left. Jaw-jerk normal. Slight weakness right lower face. Marked bilateral nerve deafness.

Bilateral wasting and weakness, left more than right, of shoulder girdle and upper arm muscles. All deep reflexes much depressed. Sensation normal. Cerebellar type of ataxia. Abdominal reflexes diminished all segments.

Marked degree of flaccid paraplegia. All deep reflexes absent. Right plantar response flexor, left equivocal. Hypæsthesia over dorsum of both feet. Gross postural loss toes both feet. Impaired vibration sense. Sphincters: urinary incontinence at times.

*Investigations.*—C.S.F. pressure 250 mm.; fluid xanthochromic. Cells 227 lymphos. per c.mm. Protein 1,200 mg.%. W.R. negative. Lange colloidal gold curve normal. Blood-count normal. E.S.R. normal. Blood W.R. negative. Plasma proteins 6.5 grammes %. X-ray chest normal.

A wide range of investigations was carried out including urinary porphyrins, brucella agglutination and complement-fixation tests, neutralization test against virus of louping-ill (Dr. Weston Hurst), muscle biopsy, and guinea-pig inoculation of C.S.F., with negative results.

## REFERENCES

- 1 BELL, T. (1783) *Quædam de Diætæ seu materia diætetica*. Edinburgh, Balfour and Smellie.
- 2 FOX, J. (1803) *The Natural History of the Human Teeth*. London. E. Cox.
- 3 HUNTER, J. (1771) *The Natural History of the Human Teeth*. London, J. Johnson. (2nd Edn. 1778.)
- 4 RAE, J. (1782) *Lectures on the Teeth*. Notes in MS. in the Library of the Royal Society of Medicine (L.9/b.19).
- 5 BELL, T. (1829) *The Anatomy, Physiology and Diseases of the Teeth*. London, S. Higley.
- 6 — (1827) On the Structure and Use of the Submaxillary Odoriferous Glands in the Genus *Crocodylia*, *Philos. Trans.* (i), 132.
- 7 — (1837) A History of British Quadrupeds. London, John Van Voorst.
- 8 BLAKE, R. (1801) *An Essay on the Structure and Formation of the Teeth in Man and Various Animals*. Dublin, William Porter.
- 9 OWEN, R., and BELL, T. (1853) *Fossil Reptilia of the London Clay*. London.
- 10 — (1840-45) *Odontography*. London. Baillière.
- 11 DARWIN, F. (1887) *The Life and Letters of Charles Darwin*. London, John Murray.
- 12 BELL, T. (1853) A History of the British Stalk-eyed Crustacea. London, John Van Voorst.
- 13 — (1840) See Darwin, C. R., *The Zoology of the Voyage of H.M.S. Beagle*, Pt. V, Reptiles. London, Smith Elder & Co.
- 14 DARWIN, C. R. (1859) *The Origin of Species*. London, Ward, Lock & Co.
- 15 WALLACE, A. R. (1880) *Darwinism*. London, Macmillan & Co.
- 16 BELL, T. (1874) *History of British Quadrupeds*, 2nd Edn. London, John Van Voorst.
- 17 — (1877) *The Natural History & Antiquities of Selborne*, edited by Thomas Bell. London, John Van Voorst.
- 18 SALTER, S. J. A. (1844) Urinary Calculus of a Peculiar Form, *Trans. path. Soc. Lond.*, 5, 203.
- 19 — (1855) Report on a Case of Calcified Pericardium, *Trans. path. Soc. Lond.*, 7, 73.
- 20 — (1857) Report on a Case of Osteo-Sarcoma, *Trans. path. Soc. Lond.*, 7, 372.
- 21 — (1853) Dentine of Repair, *Guy's Hosp. Rep.*, 8, 345.
- 22 — (1855) On the Intrinsic Calcification of the Permanent Tooth-pulp, *Guy's Hosp. Rep.*, N.S., 1, 196.
- 23 LYLE, H. W. (1935) *King's and Some King's Men*. London, Oxford University Press.
- 24 HENRY, C. B. (1943) The Hereditary Greatness of the London School of Dental Surgery, *Roy. dent. Hosp. Mag.*, 12, 17, 43, 60.
- 25 CARTWRIGHT, S. (1856-58) Lectures on Dental Surgery, delivered at King's College, London, *Brit. J. dent. Sci.*, 1, 2.
- 26 FAY, C. (1826) "Improved Forceps for the Use of Dentists," *J. Soc. Arts*.
- 27 CARTWRIGHT, S., and COLEMAN, A. (1865) Remarks upon the Collection of Skulls in the Crypt of Hythe Church, Kent, *Trans. odont. Soc., Lond.*, 4, 221.
- 28 ROBERTSON, W. (1835) *A Practical Treatise on the Diseases of the Teeth*. London, Longmans; and Birmingham, J. Belcher & Sons.
- 29 COLEMAN, A. (1861-63) On the Nature of Dental Caries, *Trans. odont. Soc., Lond.*, 3, 80.
- 30 UNDERWOOD, A. S. (1908) Discussion on Antral Disease, *Brit. med. J.* (ii), 463.
- 31 — (1910) An Inquiry into the Anatomy and Physiology of the Maxillary Sinus, *J. Anat. Lond.*, 44, 354.
- 32 WALLACE, J. S. (1926) *The Teeth and Health*. London, Faber & Gwyer.
- 33 — (1927) *Variations in the Form of the Jaws*. London, Baillière, Tindall & Cox.

All symptoms have been slowly progressive although the tremor was temporarily improved by moderate doses of belladonna.

**Examination.**—No evidence of intellectual deterioration. Speech moderately dysarthric. Slight loss of facial expression. Pupils and ocular movements full. No nystagmus. Rhythmic, coarse, static tremor of head, left shoulder, arm and hand with occasional tremor of right hand. Tremor intensified by emotion but disappears when limb is supported. On voluntary movement this coarse tremor is replaced by a less intense and more rapid intention type of tremor. Posture of hand not typical of Parkinsonism; no cogwheel phenomenon. All reflexes very brisk, including jaw-jerk. Bilateral extensor plantar responses. No sensory loss. Gait—left arm fixed across body and fails to swing. Mild spastic gait, less apparent when running.

**Investigations.**—C.S.F. normal. Blood W.R. negative. X-ray of skull normal. E.E.G. normal, including a record taken during sleep after second medication.

**Discussion.**—Dr. Gordon Holmes in 1904 described a series of eight cases which showed a static form of coarse tremor replaced by an intention tremor on voluntary movement. Some of these cases showed evidence of third nerve paralysis and unilateral or bilateral pyramidal signs. The pathological lesion was either vascular or neoplastic in the mid-brain. Dr. Holmes attributed the tremor to involvement of the red nucleus or superior cerebellar peduncle. Kremer, Russell and Smyth in 1947 published a number of cases of a mid-brain syndrome following head injury. Several of these cases showed a mild Parkinsonian facies; in addition dysarthria, ataxia, a static coarse tremor and pyramidal signs were seen in all cases. Evidence of damage to the third nerve was inconstant.

In the present case the mild Parkinsonian features may be accounted for by damage to the substantia nigra, and the tremor to a lesion of the red nucleus or its connexions. The picture shown by this patient is not consistent with a previous attack of encephalitis, nor is there any evidence to suggest a neoplasm. On the other hand the likeliest explanation appears to be trauma resulting from contusion to the mid-brain caused by one or more knockouts.

#### REFERENCES

HOLMES, GORDON (1904) *Brain*, 27, 327.

KREMER, M., RUSSELL, W. R., and SMYTH, G. E. (1947) *J. Neurol., Neurosurg. Psychiat.*, 10, 49.

**Dr. Russell Brain:** I have recently seen a very similar syndrome in a professional boxer who exhibited a mixture of torticollis, Parkinsonism and cerebellar ataxia suggesting that the main damage had fallen upon the striatum and upper mid-brain.

**Dr. Helen Dimsdale:** It is interesting that this patient complained of excessive salivation, a symptom usually associated with encephalitic Parkinsonism.

**Multiple Cranial and Peripheral Neuropathy.**—REDVERS IRONSIDE, F.R.C.P.

Miss L. D., aged 62.

She thinks that her left upper limb has never been so well developed as the right. About eight years ago she noticed that the left half of her tongue was wasted and this has become progressively worse.

One year ago: Diplopia, left-sided ptosis, and a divergent squint. At that time she was found to have a partial third-nerve and a complete sixth-nerve palsy on the left side, with impairment of sensibility to cotton-wool and pin-prick over the first and second divisions of the fifth nerve. Corneal reflex diminished on the left side. Ptosis improved but sensibility on the face has become more affected and now involves all three divisions of the left fifth nerve. The motor division does not appear to be affected.

Six months ago: Suddenly developed left foot drop with analgesia to pin-prick and cotton-wool over the outer border of the foot and the outer aspect of the left calf.

C.S.F. normal. X-rays skull normal. Blood W.R. negative.

Patient has a fibroma over the right lower ribs in front and another on the flexor aspect of the left wrist.

Dr. Ironside drew attention to the length of the history, the presence of fibromata and a developmental anomaly, and commented on the frequency with which cases of multiple neuropathy were found to be due to tumours involving nerves.

**Vestibular Syndrome with Facial Palsy.**—REDVERS IRONSIDE, F.R.C.P.

Mrs. G. B., aged 62.

For the past eleven years has had attacks of vertigo, particularly after hot baths. For the last three years the attacks have become more frequent and have lasted as long as twenty-four hours. The present attack commenced four weeks ago with severe vertigo, pain behind the

*Progress.*—August 1948 : Wasting was now apparent in the peripheral muscles of upper and lower limbs, but at the same time some return of power was noted. By the end of September nystagmus was present on direct fixation and was more vertical than horizontal. Arm reflexes were approximately normal ; tone was now somewhat increased in both legs. Right plantar response was equivocal and the left extensor.

Early in December his condition had deteriorated, incontinence was frequent, at times he was indifferent to it and was confused. Upper as well as lower limbs were spastic with increased reflexes and double extensor plantar responses.

8.12.48 : Patient became ill and drowsy, but retained consciousness. Speech and swallowing were impaired. There was conjugate deviation of head and eyes to right. Spasticity and paresis of all four limbs were intensified. Signs of a complete left hemiplegia with hemianæsthesia and hemianopia were present. A grasp reflex was obtained on the right side.

*Further progress.*—Power slowly returned in the limbs, more quickly in the upper than the lower ; the latter have remained severely paretic. A sensory level appeared at D8-9 segment. Cerebellar signs became more pronounced. Mental confusion was noted until March 1949 ; since then considerable improvement in his mental state has occurred. Except during the acute flare-up in December and on a few other isolated occasions, there has been no fever. The majority of the tests mentioned previously were repeated at intervals, and were negative.

C.S.F. : This was examined at monthly intervals until October 1948. It has shown the following features : (1) Xanthochromia. (2) Pleocytosis varying between 160 and 45 cells per c.mm., lymphocytes or polymorphs predominating. (3) Protein ranging from 1,200 to 3,500 mg. %. (4) A consistently negative W.R., and Lange colloidal gold curve. A specimen on April 20, 1949, contained 30 cells per c.mm. (28 lymphos., 2 polys.) and 400 mg. % of protein, and another on May 9, 1949, showed lymphos. 50, polys. 5, protein 350 mg. %.

Repeated attempts to isolate an organism from the C.S.F. have failed.

*Discussion.*—The diagnosis of a Guillain-Barre syndrome was at first considered in view of the four-limb flaccid paralysis and the xanthochromic C.S.F., although there were several atypical features, notably bilateral deafness and cerebellar signs. The prolonged course of the illness, the appearance of fresh encephalitic and myelitic signs a year after the onset, and the persistent pleocytosis in the spinal fluid suggested as an alternative diagnosis an obscure form of chronic encephalo-mycelo-radiculitis. The man's occupation and the fact that he had nursed a cow with fever for three months prior to the onset of his illness suggested the possibility of a chronic form of neuro-brucellosis but laboratory tests carried out under the supervision of Professor F. Selbie of the Bland-Sutton Institute have failed to confirm this diagnosis. Judging by the clinical improvement and the recent diminution in the pleocytosis and the protein content of the C.S.F. it would appear as if the active process was dying out.

*POSTSCRIPT.*—Since this case was shown, Professor Dorothy Russell has informed us of a fatal case of encephalo-mycelo-radiculitis in a cowman which showed clinical features very similar to those shown by our patient.

Dr. H. G. Miller mentioned the difficulty sometimes caused by cases of porphyria in which the biochemical abnormality may for considerable periods be limited to the excretion of colourless porphyrinogens, and asked how completely this possibility had been excluded.

Dr. Russell Brain: Blindness due to optic neuritis and deafness may both occur in acute infective polyneuritis, and so also may cerebral symptoms. In spite of its chronic course it seems to me that the whole of the clinical picture in this case may be the result of infection with a virus allied to, if not identical with, that responsible for acute infective polyneuritis.

*Mid-Brain Syndrome in a Professional Boxer.*—DOUGLAS MCALPINE, M.D., F.R.C.P., and FRANCIS PAGE, M.D., M.R.C.P.

J. N., aged 24.

A boxer since the age of 14. Had never received severe punishment in the ring, despite three months' booth boxing, until January 1948 when he was twice knocked out. Amnesia on each occasion did not exceed a few seconds.

February 1948, after losing his temper, his whole body shook and he felt as though he wanted to "get going" with his fists. This quickly subsided but two days later he noticed slight tremor of the left hand, gradually increasing in severity and, during the next few weeks, spreading up the arm to involve the shoulder and head. Excessive salivation was also noticed during this period, and in March 1948 his speech became slow and indistinct and walking unsteady.

**Dr. Douglas McAlpine:** I have under my care at the Middlesex Hospital a similar case in which symptoms have been present for eighteen months. Carcinoma has not yet been found. Despite the length of history in these two cases of sensory neuropathy, malignant disease cannot be excluded.

**Dr. David Kendall:** I have seen two patients suffering from a condition similar to the one presented in each of whom carcinoma of the stomach was found. Could not the same condition be present in this case, the achlorhydria being significant? It is of some interest that Denny-Brown's first case was found to have involvement of the cardiac end of the stomach by a lung tumour.

**Optic Atrophy. Diabetes Insipidus. Cause Undetermined.**—W. RUSSELL BRAIN, D.M.

H. B., aged 26.

Two and a half years ago: Just before discharge from R.A.F. he noticed onset of increasing thirst. Recently he has required as much as 12 pints of water a day.

One and a half years ago: Noticed flashes of coloured lights in front of his eyes, sometimes a series of red dots followed by a series of blue ones.

One year ago: Noticed that vision in R.E. had almost disappeared to a dim central vision. He also became aware of defect of colour vision (green for red).

Six months ago: Suddenly began to see everything as green. If he sits down to a book he may fall asleep within five minutes, but otherwise has noticed no tendency to somnolence. Vision in the left eye has recently become less distinct. He has lost 4 st. in weight in the last four years.

October 1948: Admitted to the London Hospital.

*Family history.*—Great-grandfather had excessive thirst.

*Personal history.*—Married, two children, Some lessening of libido in recent months.

*On examination.*—Co-operative and intelligent. No obesity. No pallor or external abnormality of the skull. Tongue furred. No speech defect.

Cranial nerves: No anosmia. Fundi—bilateral primary optic atrophy, right more than left. Vessels normal. Can only recognize people within 8 feet. Visual acuity R. 6/60, L. 6/18, uncorrected. Pupils equal but show sluggish reaction to light on the left. Visual fields—right side greatly constricted. Left side less severely constricted. External ocular movements full. Coarse nystagmus right and left.

Other cranial nerves N.A.D.

No motor or sensory loss. Gait normal.

Reflexes: Arm-jerks slightly brisker right than left. Plantars flexor.

Other systems: N.A.D.

*Investigations.*—Lumbar puncture: Pressure 140. Free rise and fall to jugular compression on either side. Protein 40 mg. % 4 cells. Blood and C.S.F. W.R. negative.

Lange 001111.

Polyuria was satisfactorily controlled with pituitrin, and finally balanced with injections of pitressin tannate 1 c.c. i.m. on alternate days.

Air encephalogram: 45 c.c. of air. This showed air over the posterior surface of the chiasma and infundibulum.

23.11.48: Ventriculogram: No abnormality detected.

6.12.48: Vision appeared to be deteriorating. V.A.R. 6/60, V.A.L. between 6/12 and 6/18. Extensive colour vision tests were conducted which showed that his colour blindness was of the tritanopic type, and differed in several important respects from the congenital type of deuteranopia.

Gastric test meal: N.A.D.

Hæmoglobin 99%. Normal cell count.

Blood cholesterol 162 mg. per 100 c.c.

Since discharge on 10.12.48 polyuria has been well controlled, but the right eye is now almost blind, and the left has very indistinct vision.

*Investigations.*—Lumbar puncture: Pressure 90. 2 cells, protein 40 mg., chlorides 800 mg., sugar 83 mg. per 100 c.c.

V.A.L. 6/36. Left visual field shows severe constriction to 15/2,000 white. Right visual field—hand movements only. Both fundi show severe primary optic atrophy. Retinæ normal.

*Subsequent note.*—Exploration by Mr. D. W. C. Northfield revealed no tumour. The optic nerves were pinker than normal. The pia arachnoid around them was adherent to the neighbouring structures, but this appeared to be secondary to the inflammation of the nerves themselves.

left ear and vomiting. After a few days, left facial paralysis developed with impairment of taste on the anterior two-thirds of the tongue. She has become slightly deaf in the left ear. Ear drums and mastoids normal.

C.S.F., on admission, 65 lymphos. per c.mm., and 80 mg.% protein. Cultures sterile. W.R. negative in blood and C.S.F.

Mr. C. S. Hallpike reports a very slight bilateral high-tone deafness. Marked ataxia with tendency to fall to the left. A preponderance of optokinetic nystagmus to the right. Caloric responses show a preponderance to the right with a reduction in the response on the left side.

The facial palsy is improving. There is no impairment of sensibility on the face or diminution of the corneal reflex. C.S.F. examination on 19.4.49 showed 77 lymphocytes per c.mm., 40 mg.% protein. She has at no time shown herpetic vesicles on the skin or in the mouth or nose. (On 9.6.49 C.S.F. analysis had become normal.)

Dr. Ironside said the case was probably one of a long-standing slowly progressive labyrinthine degeneration. There appeared to have been a recent superimposed infection as evidenced by the rapidly clearing facial palsy and pleocytosis in the C.S.F. There was no evidence that the infection was pyogenic. He had observed other cases of vestibulo-facial syndrome, one with recurrent attacks of vertigo and facial palsy, probably infective in origin.

Dr. Douglas McAlpine: This would seem to be a case of geniculate herpes sine herpes.

Dr. H. G. Miller suggested that this might be a case of herpes zoster, mentioning similar patients in whom a definite eruption gave a clue to the nature of an encephalomyelitis with cranial nerve lesions. The diagnosis might be clarified by serological tests.

**Primary Sensory Neuropathy.**—S. NEVIN, M.D., and L. G. KILOH, M.B., M.R.C.P.

H. D., male aged 38.

October 1947: Noticed numbness in left leg. Two months later—shooting pains and tenderness in this limb.

February 1948: Symptoms more severe, left leg clumsy and difficult to control. The right arm became similarly involved.

May 1948: Left arm numb, followed by pain, tenderness and great clumsiness.

September 1948: Abdomen, chest and back became numb. Numbness of right leg with subsequent clumsiness.

December 1948: Symptoms maximal. Unable to walk without assistance, grossly ataxic and unable to feed himself. Appetite poor. Nauseated by food. Lost 5 pounds in weight. He is impotent.

*On examination.*—Cranial nerves normal apart from impaired sensation in distribution left fifth nerve.

No wasting or weakness except of left hand (following tendon injury 1942).

Extreme hypotonia. Gross ataxia and inco-ordination of arms and legs—worse with eyes closed.

All tendon reflexes absent. Abdominal reflexes decreased in upper quadrants, absent in lower. Plantar reflexes flexor.

Sensation: Light touch lost in upper limbs; in distribution T6–11 and below knees. Elsewhere diminished except left thigh. Pain and temperature sensation markedly impaired hands and feet and in distribution T6–12, impaired upper chest, upper limbs and below knees. Generalized increase of muscle tenderness. Sense of passive movement absent in all limb joints, normal in neck. Vibration sense absent in and below clavicles.

C.S.F. (March 1948): Protein 120 mg.%. Now normal.

Histamine-fast achlorhydria. Gastroscopy normal. Occult blood negative.

X-ray chest and tomograms of hilar regions—N.A.D.

Electrical reactions and electromyography of numerous muscles—N.A.D.

Biopsy peripheral nerve—intense degeneration. Muscle normal.

This case appears to have the same features as those described by Denny-Brown as Primary Sensory Neuropathy (1948), both of which were associated with carcinoma of bronchus. In this case there is no evidence of a carcinoma of any sort. Denny-Brown thought that pantothenic acid deficiency might be implicated. The present patient has been given pantothenic acid and other members of the vitamin-B group. His symptoms have not improved but neither have they progressed.

#### REFERENCE

DENNY-BROWN, D. E. (1948) *J. Neurol., Neurosurg. Psychiat.*, **11**, 73.

## Section of Laryngology

President—E. COWPER TAMPLIN, M.C., F.R.C.S.Ed.

[March 4, 1949]

### The Present Position in the Surgical Treatment of Carcinoma of the Thoracic Gullet

By C. P. WILSON

THE treatment of carcinoma of the thoracic gullet was first undertaken by the general surgeons and apart from blind bouginage—at that time perhaps the most merciful form of treatment—it consisted merely of palliative gastrostomy.

The first step in the progress of treatment came as a result of the introduction of œsophagoscopy and it naturally followed that the disease came into the province of the laryngologist.

Unfortunately progress in treatment was limited to what the endoscopist could undertake through the confines of the œsophageal speculum but I do not think we need be ashamed of the many diverse and often ingenious methods which have been tried to utilize as fully as possible the advantages which direct inspection of the growth could give.

Even though we may now be forced to accept the conclusion that endoscopy by itself can only give us facilities for diagnosis and a means of affording palliation, we should not on that account belittle the many efforts which have been made during the century to attain the possibility of cure.

Most of our efforts to cure have been based on some form of radiotherapy; first a tube of radium, then implantation of radon seeds into and around the growth, and later the use of teleradium or deep X-rays in large fields or in multiple fields, either alone or combined with local irradiation with radium emanation; there is no question but that the technique of radiotherapy is still improving. Some good has been done by these methods and there are scattered reports of occasional cures, but the statistical records of series of cases of any size are poor reading and the mortality rate of our cases treated by such means is in the neighbourhood of 100%.

In saying this I am not belittling the work which has been done by the radiotherapists and I have on several occasions during the last twenty-five years become enthusiastic over some particular method of treatment because of the promising results obtained associated with temporary disappearance of the growth and relief for one, two or even more years, but if we talk of five-year cures in other types of carcinoma we cannot talk in terms of one- or two-year cures in carcinoma of the gullet.

Although this disease had more or less come into our own province the surgeons had not given up hopes of dealing with cancer of the gullet surgically; even as long ago as 1870 Bilioth had been endeavouring to work out a technique in animals—in his case particularly in respect of the cervical gullet—but it was not until 1913 that Torek was successful in curing a patient by means of a transthoracic œsophagectomy.

# Hereditary Optic Atrophy in Family with Keratoderma Palmaris et Plantaris (Tylosis).— HELEN DIMSDALE, M.D.

W. S., aged 61. Four years ago central vision of both eyes became misty, left more than right. Vision deteriorated rapidly for two months, until he became unable to read large print. Examination two months after the onset of visual failure showed slight temporal pallor of the left optic disc, the right disc was normal. V.A.R. 3/60. V.A.L. 3/60.

There was a paracentral scotoma in the right visual field, and a large central scotoma in the left visual field with some reduction of peripheral vision to 5/2,000 white. The reaction of the pupils to light was ill-sustained. Three months later both discs were atrophic with slight haziness of their margins.

Since then the vision of the left eye has deteriorated to 1/60 and the scotoma has broken through in an upward direction to the periphery. Colour vision of both eyes for red and green is virtually absent.

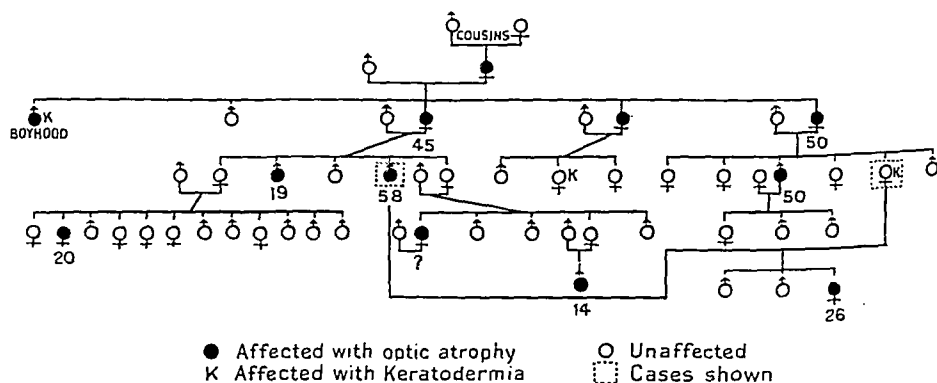


FIG. 1.—Family tree of W. S. The figures show the age of onset of the disease.

**Family history.**—His great-grandparents were first cousins (see fig 1). On the female side grandmother, uncle, mother, two aunts, eldest brother (examined), son of affected aunt, daughter of normal eldest sister, normal younger sister's daughter, and her grandson by a normal daughter are stated to have been affected by the disease. The patient married his first cousin, the daughter of his affected aunt, and has had two sons and a daughter. One son aged 5 died of diphtheria and one son aged 34 is normal. A daughter aged 27 is under the care of Dr. S. Behrman, and I am grateful to him for the information that she is an example of the disease. There are no grandchildren.

The patient's wife (cousin) has thickening of the palms and soles with fissuring. She attended at Dr. O'Donovan's Outpatients at the London Hospital some years ago. Another female cousin has thickening of the skin of the ears as well as of the palms and soles. The patient's uncle with visual failure had thickening of the palms.

**Comment.**—The family is unusual in that 7 out of 12 cases of optic atrophy were females. The mode of inheritance would appear to be sex linked, with irregular dominance in the heterozygous female. Keratoderma palmaris and plantaris is recognized by dermatologists as a heredo-familial cutaneous disorder which may be recessive or dominant. A form known as "Mal de Meleda" in which hyperkeratosis extends on to the dorsum of the hands and feet occurs among the inhabitants of an island off the coast of Dalmatia, where there has been intermarriage for a century.

I am indebted to Dr. W. J. O'Donovan for advice on the nature of the skin lesions in this family, and to Dr. S. P. Meadows on whose behalf I first saw the patient at Moorfields Eye Hospital.



V. E. Negus said that if they wished to decide whether it was right and proper to refer these cases for operation and to determine what this entailed in suffering to the patient, it was useful to review the methods that had been adopted and come to some conclusions. His own feeling was that the position was now much more favourable than formerly.

The route now adopted by most surgeons to remove a carcinoma of the œsophagus was trans-thoracic.

Before he embarked on this operation the surgeon must have formed some impression as to the character of a growth; œsophagoscopy was obviously essential. Another point was whether the growth was adherent to the trachea or bronchi and whether there were secondary glands present. By passing a bronchoscope one could determine whether there were glands at the bifurcation of the trachea, or whether there was any deformity of the bronchial walls indicating that other mediastinal glands were present, showing immediately that there were no prospects of cure; but even that did not mean that the indications for operation were absent.

By the transthoracic route exposure was extremely good and the surgeon, if he preferred, could do all the work through the thorax. The exposure was certainly remarkable and sufficient to decide whether it was possible to remove a growth. Even fixation to the pleura was not a complete contra-indication to such an operation. In a recent case operated on by Mr. Muir the growth was fixed and secondary deposits were thought to nullify any prospect of cure. It was found possible, however, to bring the stomach up through the diaphragm and to anastomose it to the œsophagus above the growth. That gave the patient the ability to swallow by the normal route with more comfort than was afforded by gastrostomy. This seemed to be a considerable advance as a palliative operation.

Again, supposing the patient were found to have mediastinal glands, making the prospect of permanent cure very poor: even so it was the opinion of some surgeons that excising the growth of the œsophagus, then bringing the stomach up and anastomosing it to the free upper end of the œsophagus, was worth while, because the patient finished his days with ability to swallow by the normal passages, although he might still die from recurrence in the mediastinum.

Thirdly, a favourable growth might be removed successfully with a reasonable prospect of cure. The method could be carried out entirely through the thoracic incision, with spreading of the ribs, or by removal of two ribs if necessary, and by dividing the diaphragm the operation could be extended to the glands of the stomach and a partial gastrectomy carried out. In a recent case referred to the speaker and operated on by Mr. R. C. Brock the whole of the spleen and half the pancreas were removed, the remaining portion of the stomach was mobilized and brought up to the divided end of the œsophagus and a perfect result was obtained, enabling the patient to swallow a couple of days after the operation and to be out of bed in six days, a remarkable achievement.

The question arose of peptic ulceration following the operation. Was it likely that an anastomosis to the stomach would result in ulceration of the œsophagus, with pain and later with cicatricial contraction? In the opinion of some surgeons it was better not to use the stomach for the purpose of anastomosis. This, however, involved extra difficulties in connexion with the vascular supply through the mesentery. Other methods were employed, such as the bringing up of a loop of ileum under the chest wall, with anastomosis to the pharynx, having removed the œsophagus; and the antethoracic skin tube was still employed by some surgeons.

All this pointed to the great advantage of restoring the œsophageal continuity. His conclusion was that every patient who was not in too bad a state of health, and in whom, after direct examination, the possibility of excision presented itself, should be referred to the thoracic surgeon, or whoever it might be who was to carry out this operation. There was sometimes a feeling that the patient would be exposed to undue suffering; that had not been his experience. As a result of the operation the patients were offered the prospect of restoration of normal swallowing, a great boon to them after their long discomfort, and in a few cases there was a prospect of cure. Therefore he felt that early œsophagoscopy and bronchoscopy were essential and that one should not hesitate to ask the surgeon, if he was prepared to do an operation, to attempt it in a proportion of these cases.

A. Dickson Wright said that carcinoma of the œsophagus had by its difficulties attracted the attention of many surgeons of which he had been one. It was hard to fit it into any speciality, lying as it did in the province of the throat, the thoracic and the gastric surgeon, and towards the accomplishment of surgical removal all three had made a contribution. For instance, the dilatation of the œsophagus or the insertion of a Souttar's tube would, by giving the patient two or three weeks of glorious gluttony, fit him better for operation than any elaborate intravenous feeding. The technique of opening and closing the thorax safely and expeditiously had come from the thoracic surgeon and the mobilization of the stomach to fill the œsophageal gap from the gastric surgeon. Several surgeons (Torek, Grey Turner) had discovered how to mobilize the œsophagus from both ends.

Now that surgical removal was possible with a reasonable mortality rate, early diagnosis became more and more important so that the patients were in good condition. Once the patient had presented himself with dysphagia (substernal pain and belching immediately after swallowing) there was a strong indication for careful investigation by X-ray and œsophagoscopy. Both methods were very fallible and the radiologist should use every trick at his disposal to find the early case. The barium emulsion should be thickened to semi-solidity, barium capsules should be used, and screening while swallowing in the Trendelenburg position might also be employed. Above all, a picture of the fundus of the stomach should be made with the patient on his back and the feet elevated so as to disclose abnormalities of the gastro-œsophageal junction. Œsophagoscopy should be repeated until all

After œsophagoscopy the next step in advancement came with the introduction of intra-tracheal positive pressure anæsthesia and I do not think we can put too high a value on anæsthetic improvements in the pursuit of our aim to cure. Improvement in anæsthesia encouraged the general surgeons once again and during the time we were struggling with radiotherapy and endoscopy, pioneers of œsophageal surgery in this country such as Grey Turner and Gordon-Taylor, and Garlock in America, were fighting an uphill battle to improve their technique with the object of curing the disease by resection of the gullet.

Improvements in anæsthesia, together with methods of combating shock such as blood transfusion, were a great stimulus but with the brilliant exception of Torek's famous case in 1913 the early results were disastrous and we must honour those early pioneers who continued their work in the face of bitter disappointment and disaster by admitting that it is upon the basis of their failures that the present-day technique of œsophageal surgery has been built. In the earliest days the ultimate aim was resection of the whole gullet with pharyngeal fistula and a gastrostomy, and later an extrathoracic artificial gullet joined to pharynx above and stomach below.

During the twenty-year period after the end of the first world war several cases were recorded of successful resection and with restoration of something approaching the normal function of swallowing.

It was not only the general surgeons who took advantage of the possibility of opening the chest; we laryngologists also explored the possibility of an approach to the gullet through the pleura with the object of inserting radon seeds around the periphery of the growth in addition to treatment via the lumen and it is with pleasure that I recall assisting my late friend and chief F. J. Cleminson in performing three thoracotomies for this purpose about 1928.

The advent of the sulphonamides was a further great boon in the surgery of this region as leakage and sepsis still remained the great bugbears even when the surgical technique had been evolved to the point of being able to overcome the great shock necessitated by such extensive operative interference, and it appeared about 1938 that the limit of technical achievement had been reached with Garlock's report of three consecutive successes by Torek's technique.

What is perhaps the most dramatic change in technique has gradually been evolved during the last ten or twelve years. This is the realization of the extent to which the abdominal viscera could be mobilized to aid in restoration of continuity of the alimentary canal. Having started by pulling some of the stomach up into the thorax to enable direct suture to be undertaken in cases of resection of the lower end of the gullet, mobilization of the bowel was gradually utilized for growths of the middle part and it appears that it may be extended even further.

Our own contribution to the cure of this disease must be in aiding in its early diagnosis and passing on to those surgeons capable of dealing with such operations all those cases which are sufficiently early to be considered as operable. The inoperable cases will doubtless remain for us to relieve and palliate as best we can and it is in these inoperable cases that we must decide whether alternative methods of treatment such as radiotherapy are worthy of our consideration. Certain it is that at the present time surgery does give a hope of cure in early cases which alternative methods of treatment do not give, and we have no right, in a case which is operable, to withhold from a patient his only likely possibility of cure.

E. D. D. Davis said that he had had the opportunity of seeing Mr. R. H. Franklin and Mr. C. Price Thomas perform operations for transthoracic excision of carcinoma of the œsophagus. The technique was suitable not only for growths of the œsophagus but for congenital atresia, perforations of the œsophagus and mediastinal abscess, impassable strictures and the short œsophagus or thoracic stomach.

Mr. Wilson had emphasized the great importance of early diagnosis. It was also necessary to determine the exact position of the growth. The squamous carcinoma of the middle third of the œsophagus was more favourable for excision than the more malignant adenocarcinoma of the cardiac end of the œsophagus which was frequently an extension of a growth from the cardia of the stomach.

An early diagnosis could be made by repeated examinations with the X-ray screen and photographs. The œsophagoscope, of course, should be used more frequently and whenever there was any suspicion of œsophageal obstruction.

The majority of patients did not consult a doctor until too late and only when obstruction had been present for some time.

One of the earliest symptoms of carcinoma of the lower end of the œsophagus was epigastric pain on swallowing. Another early symptom was occasional difficulty in swallowing particularly when a large bolus of food became impacted; this was followed by a few weeks or so of no obstruction. He had not found hiccough an early symptom.

## Section of Urology

President—TERENCE J. MILLIN, M.A., M.Ch., F.R.C.S.

[May 19, 1949]

### Management of the Patient with Anuria

By ASHTON MILLER, F.R.C.S.

It is not my intention to go into the details of recent advances in the use of dialysis in the treatment of uræmia, because this has been admirably done in this Section by Reid and Darmady (1948). I am more concerned to consider the general management of a case of renal failure and the indications for the use or avoidance of dialysis. During the past two years I have had the opportunity in Bristol of observing ten cases of this type and this paper represents conclusions reached after trying various methods of treatment. In all these cases I have had the co-operation and help of Dr. G. K. McGowan of the Department of Pathology, who has done a great amount of work in performing numerous blood chemical analyses and in interpreting the results. There is no doubt that the clinical condition of the anuric patient gives little indication of the real state of affairs. It has been said that such a patient may appear to be "in vibrant health in the ward but be practically dead in the laboratory", and this is no exaggeration for astronomical blood urea values are quite compatible with a conscious co-operative patient.

To treat renal failure one must be aware of its possible causes if only to make sure that any such cause is not a continuing factor in its maintenance. Swift Joly classified 3 main causes—Pre-renal, renal, and post-renal.

By *pre-renal* he meant the stoppage of urinary secretion resulting from a fall in blood-pressure below the level which can maintain an adequate filtration pressure in the glomeruli. It has been shown that if the systolic blood-pressure in the afferent glomerular vessels falls below 40–60 mm. of mercury then secretion of urine ceases; this is equivalent to a drop of aortic systolic pressure to between 70 and 100 mm. of mercury, which can easily occur during any prolonged or traumatic operation. Moreover, one-quarter of the cardiac output goes to the kidneys, so that the effect on them of a drop in pressure is very great. The cause of the drop in blood pressure may be a fall in the circulatory blood volume, such as occurs in shock, hæmorrhage or dehydration, or to slowing of the circulation rate in cardiac failure.

By *renal* causes, he referred to any process in the kidney which stops secretion of urine in the presence of an adequate filtration pressure, and this includes the various changes which lead to tubular damage or blockage, such as all the varieties of Lucké's "Lower nephron nephrosis" (1946), and poisons affecting the renal tubules. The mechanism of this variety of anuria is still debated; some varieties have been shown to be due to tubular blockage, such as that caused by mercury poisoning and, possibly, mismatched transfusion anuria, but evidence of blockage in other cases is lacking and it seems probable that the glomerular filtrate is reabsorbed direct into the blood owing to the absence of cells lining the tubules. It is seldom an absolute anuria, but the very small amount of urine that is produced is usually of no significance. The third group of causes is *post-renal*, which implies ureteric obstruction. I believe it is essential to include these causes in any discussion of anuria although they are not strictly disturbances of secretion, because often it is not possible in the early stages to determine whether the cause is renal or ureteric. For example, in sulphonamide anuria, the most usual place for blockage to occur is at the lower ends of the ureters, but another type may occasionally appear where the blockage appears to be in the tubules and the ureters are unobstructed; as the treatment of these two varieties is different it is necessary to differentiate them as early as possible. Again, after a pelvic operation during which there has been a fall of blood-pressure, it is impossible to tell in the early stages whether anuria is due to accidental ureteric obstruction or to a true pre-renal anuria caused by continued low blood-pressure.

The functions of the kidney which are lost are:

(1) *The power of excreting water.*—This means that the skin, lungs and bowel remain as the only means by which the body can get rid of excess water and the total amount excreted by these channels does not normally exceed 1,000 c.c. per day.

(2) *The excretion of the products of protein breakdown* of which urea forms the bulk and is the most easily measured indicator.

(3) *The maintenance of the normal electrolyte balance and osmotic pressure of the blood* by excretion of excess acid or base as required, and variation of amounts of fluid reabsorbed.

doubts are cleared up. The use of pentothal and curare removed, in great part, the dangers of the procedure, although local anæsthesia was preferred because it was safer and it also gave one some idea of the patient's morale for the ordeal ahead. Biopsy should be made at the time of the examination and the stricture stretched with bougies and if possible a Souttar's tube inserted. The next two to three weeks can be used in extracting teeth, and getting the blood hæmoglobin, protein and vitamin levels up to normal totality and to improving the nutrition and strength of the patient during the period of improved swallowing. This period of good swallowing also clears up the fætor and the œsophagitis above the stricture.

Mr. Dickson Wright said that the operation he favoured for growths of the upper three-quarters was to make the first incision above the clavicle, divide the sternomastoid and mobilize the œsophagus from above as far down as possible. The next step was to open the abdomen and mobilize the stomach, leaving it nourished by the vessels running parallel to the pylorus. This completed, the lower end of the œsophagus was then freed from its diaphragmatic attachments and mobilized as high as the finger could reach and, as the last step, the opening in the diaphragm was enlarged to the size of the hand. The omentum could be left in the abdomen or brought up with the stomach, but it was tidier to leave it behind. The incision was then closed and the patient given a little rest and then turned upon his left side and the chest opened by removing the seventh rib. The intrathoracic work was reduced to a minimum by the mobilization of the œsophageal ends and it only remained to free the growth, which should be done under vision.

A small piece of the bronchus sometimes has to be removed and on one occasion a strip of the side of the aorta was resected and repaired. Mediastinal glands are removed and also a very important group at the cardia. The appropriate portion of the œsophagus (and stomach) is now resected in the thorax. The making of the final anastomosis need not be considered in doing this. The neck wound is now reopened and the upper end of the œsophagus withdrawn and the fundus of the stomach delivered on the neck and the anastomosis made *en plein air*. The stomach and œsophagus are now returned to the chest and a few anchoring stitches put in place and the thorax closed and the patient turned upon his back and the neck wound is finally closed using suction catheters through this wound to re-expand the lungs.

In the event of inoperability, radon seeds can be used around the growth in a few cases and in others the patient can eke out his days with the Souttar's tube, or in others the fundus of the stomach can be brought up and anastomosed to the side of the œsophagus above the growth.

For operation on the lower end of the œsophagus and cardiac end of the stomach, the operation was performed through a transverse incision in the epigastrium extending up into the chest over the eighth rib and with the chest wall open and the diaphragm divided, the exposure was excellent and the anastomosis was made inside the thorax, using stomach remains or a mobilized length of jejunum to join with the divided end of the œsophagus.

After operation, blood transfusion, antibiotics, rectal water, routine chest X-rays and bronchoscopic suctions prevent the post-operative deaths of olden days. With early diagnosis, careful pre-operative preparation and extreme post-operative vigilance, the mortality rate was becoming quite reasonable.

C. P. Wilson, in reply, said that there was one point which had not been mentioned but which he thought was very important both to themselves and to general surgeons. This was the elasticity of the gullet. A mistake was occasionally made in thinking that a growth was much further down the gullet than it actually was, because when an œsophagoscopy was done the gullet was pushed down just as much as the growth itself and the gullet was always longer if one had an œsophagoscope in it. General surgeons, he thought, stretched the gullet when they exposed the growth and started to pull it down. It had always been a source of amusement to him when he had seen a specimen of a growth that had been removed, because it was almost a standard thing for the surgeon to say "of course it has all shrunk up now; there appears to be only about half an inch of gullet above the growth but I can assure you there was 3 inches at the time".

One had to make quite certain that the division of the gullet was really well above the growth and not apparently so on account of the stretching that had taken place.

## Section of Urology

President—TERENCE J. MILLIN, M.A., M.Ch., F.R.C.S.

[May 19, 1949]

### Management of the Patient with Anuria

By ASHTON MILLER, F.R.C.S.

It is not my intention to go into the details of recent advances in the use of dialysis in the treatment of uræmia, because this has been admirably done in this Section by Reid and Darmady (1948). I am more concerned to consider the general management of a case of renal failure and the indications for the use or avoidance of dialysis. During the past two years I have had the opportunity in Bristol of observing ten cases of this type and this paper represents conclusions reached after trying various methods of treatment. In all these cases I have had the co-operation and help of Dr. G. K. McGowan of the Department of Pathology, who has done a great amount of work in performing numerous blood chemical analyses and in interpreting the results. There is no doubt that the clinical condition of the anuric patient gives little indication of the real state of affairs. It has been said that such a patient may appear to be "in vibrant health in the ward but be practically dead in the laboratory", and this is no exaggeration for astronomical blood urea values are quite compatible with a conscious co-operative patient.

To treat renal failure one must be aware of its possible causes if only to make sure that any such cause is not a continuing factor in its maintenance. Swift Joly classified 3 main causes—Pre-renal, renal, and post-renal.

By *pre-renal* he meant the stoppage of urinary secretion resulting from a fall in blood-pressure below the level which can maintain an adequate filtration pressure in the glomeruli. It has been shown that if the systolic blood-pressure in the afferent glomerular vessels falls below 40–60 mm. of mercury then secretion of urine ceases; this is equivalent to a drop of aortic systolic pressure to between 70 and 100 mm. of mercury, which can easily occur during any prolonged or traumatic operation. Moreover, one-quarter of the cardiac output goes to the kidneys, so that the effect on them of a drop in pressure is very great. The cause of the drop in blood pressure may be a fall in the circulatory blood volume, such as occurs in shock, hæmorrhage or dehydration, or to slowing of the circulation rate in cardiac failure.

By *renal* causes, he referred to any process in the kidney which stops secretion of urine in the presence of an adequate filtration pressure, and this includes the various changes which lead to tubular damage or blockage, such as all the varieties of Lucké's "Lower nephron nephrosis" (1946), and poisons affecting the renal tubules. The mechanism of this variety of anuria is still debated; some varieties have been shown to be due to tubular blockage, such as that caused by mercury poisoning and, possibly, mismatched transfusion anuria, but evidence of blockage in other cases is lacking and it seems probable that the glomerular filtrate is reabsorbed direct into the blood owing to the absence of cells lining the tubules. It is seldom an absolute anuria, but the very small amount of urine that is produced is usually of no significance. The third group of causes is *post-renal*, which implies ureteric obstruction. I believe it is essential to include these causes in any discussion of anuria although they are not strictly disturbances of secretion, because often it is not possible in the early stages to determine whether the cause is renal or ureteric. For example, in sulphonamide anuria, the most usual place for blockage to occur is at the lower ends of the ureters, but another type may occasionally appear where the blockage appears to be in the tubules and the ureters are unobstructed; as the treatment of these two varieties is different it is necessary to differentiate them as early as possible. Again, after a pelvic operation during which there has been a fall of blood-pressure, it is impossible to tell in the early stages whether anuria is due to accidental ureteric obstruction or to a true pre-renal anuria caused by continued low blood-pressure.

The functions of the kidney which are lost are:

(1) *The power of excreting water.*—This means that the skin, lungs and bowel remain as the only means by which the body can get rid of excess water and the total amount excreted by these channels does not normally exceed 1,000 c.c. per day.

(2) *The excretion of the products of protein breakdown* of which urea forms the bulk and is the most easily measured indicator.

(3) *The maintenance of the normal electrolyte balance and osmotic pressure of the blood* by excretion of excess acid or base as required, and variation of amounts of fluid reabsorbed.

### Spontaneous Recovery

It is usually about the eighth day after the onset of renal failure that urine secretion begins again, and this is thought to be due to regeneration of the cells lining the tubules; the kidneys are capable of supporting life about the fourteenth day or a little later. The first urine that is produced is very dilute and is little more than a glomerular filtrate containing numerous casts and much protein, but slowly the power of concentration returns until renal function tests reach normal limits in some cases.

We can, therefore, resolve the course of the condition into three phases, as Muirhead (1948) has suggested: the first, in which renal failure is determined and which lasts a few hours or less, the second, in which life continues in the absence of renal function, the blood urea mounting daily and electrolyte disturbances gradually increasing, and the third phase, in which renal recovery starts and continues with resultant diuresis and excretion of large quantities of salt in what is almost a glomerular filtrate. In other words, the kidneys recover spontaneously or not at all by a normal process of healing of damaged epithelium.

If one accepts this explanation of the course of the condition, then obviously when the kidneys are not working, fluids must not be given in excess of one litre each day and no attempt should be made to force the kidneys to secrete which interferes with the water and salt balance, or which prevents regeneration of tubular epithelium.

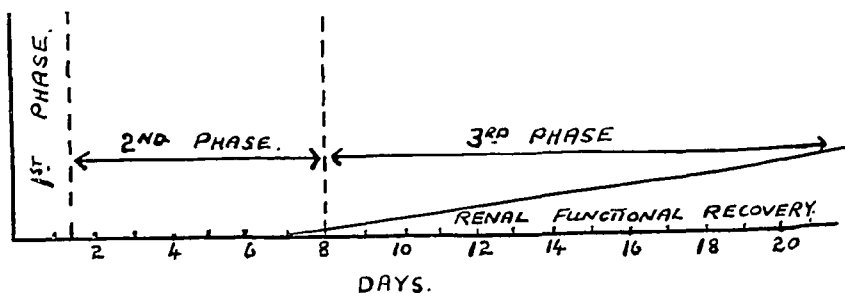


FIG. 1.—Three-phase management.

We have come to the conclusion that these two principles are the basis of successful management of temporary renal failure. As a result of unsuccessful efforts made in earlier cases I can fully endorse Lattimer's view (1945) that patients who have been given excess fluid in the early stages show a worse prognosis and take longer to show recovery of urine secretion; and the striking results of Coller (1948) demonstrate this: out of 10 cases, the first 5, treated by "forcing fluids", all died, while the second 5 all lived when fluids were restricted. Giving excess fluid causes dilution of the body fluids, resulting in clinical oedema; and it is useful to remember that oedema does not make its appearance until there is considerable dilution, as the blood picture of this case shows; there was only moderate clinical oedema:

| P. P., AGED 20 YEARS. ANURIA 8 DAYS |                   |                    |                  |              |               |                    |                    |
|-------------------------------------|-------------------|--------------------|------------------|--------------|---------------|--------------------|--------------------|
| Sodium<br>mg. %                     | Chloride<br>mg. % | Bicarb.<br>vols. % | Calcium<br>mg. % | Protein<br>% | Urea<br>mg. % | Potassium<br>mg. % | Phosphate<br>mg. % |
| 275<br>(330)                        | 360<br>(600)      | 40<br>(60)         | 6.8<br>(10)      | 5.9<br>(6.5) | 350<br>(30)   | 28<br>(18)         | 7.5<br>(3)         |

(Figures in brackets represent normal levels.)

### Early Methods of Treatment

In our early cases every effort was made as soon as possible to persuade the kidney to function not only by giving fluids, but also by administering diuretics; the most potent of these is sodium sulphate in 4.285% solution, which in ordinary circumstances can be relied upon to produce a profuse diuresis. We did not realize, however, that if the kidney is not producing urine, this solution cannot have any effect other than increasing the circulatory blood volume, and the levels of sodium and sulphate in it; none is excreted except when it is washed out in the glomerular filtrate as a foreign substance which is not reabsorbed in the tubule. It was also found that administration of this salt made it difficult to determine the chloride and bicarbonate levels of the blood. All other diuretics require secretion to be proceeding to produce any result, and were therefore abandoned. Further activity was directed towards increasing the blood supply of the glomeruli and tubules by one of the methods of paralysing the sympathetic supply of the kidney. This can be done by administering a spinal anaesthetic, but as this must reach as high as the level of the

sixth thoracic segment to be effective, it has been avoided for fear of the almost inevitable drop in blood-pressure; epidural anaesthesia has the same disadvantage, so lumbar paravertebral sympathetic block has been preferred. This has been performed in 5 cases at varying stages of the condition without any effect on secretion, though we have achieved vasodilatation in the leg. As with the tetra-ethyl ammonium salts, it is probable that by the time that the need for their use is obvious, secondary tubular damage has already occurred and vasodilatation will be without effect.

Decapsulation of the kidneys has been used in 3 cases, also without effect. There are two reasons given for employing this operation, either to increase the blood supply of the renal cortex or to remove the sympathetic supply to the renal cortical vessels. If anything a very slight diminution in blood supply is all that is attained because the minute vessels passing into the interstitial tissue from the cortex are torn, and any revascularization must be achieved by the formation of granulation tissue which will take many days to be effective. The sympathetic supply enters the kidney along the renal vessels and the cortex contains no nerve tissue. It has also been suggested that it may be used when there is great oedema present on the supposition that it allows oedema fluid to pass out from the substance of the kidney and so diminishes the obstructive pressure on the glomeruli and tubules. Though fluid may drain out and the intrarenal pressure may fall, oedema will still be present because the condition is generalized and is the result of an overloaded circulation. The cases on which this operation was tried included a patient with renal cortical necrosis and another with the lower nephron syndrome resulting from incompatible blood transfusion; in the former case there had been gross overhydration and generalized oedema was present, the operation being performed on the fifth day of anuria with the blood urea 200 mg.%; this therefore represented a fair test of the operation as the patient was still in a fairly good condition. Though much fluid drained through the incisions, there was no decrease in the general oedema during the next two days, no urine was produced, the blood urea rose to 230 mg.% and she became comatose. Sections of the kidney taken at the time of the decapsulation and at autopsy later showed a massive necrosis of the cortex exactly resembling an infarct of the kidney. It is impossible to believe that the operation achieved anything helpful in this case. In the other case renal failure was far advanced, the blood urea had reached 290 mg.% after seven days of complete anuria; where now I would unhesitatingly use peritoneal dialysis, I performed a quick bilateral decapsulation and the patient died four hours later. In a third case of advanced uraemia due to a sudden exacerbation of chronic nephritis with anuria, bilateral decapsulation produced no result and the patient died a few hours afterwards. So that, although it is true that the operation need not be formidable and can be done very expeditiously with minimal inhalation anaesthesia, I am convinced that successes claimed for it are fortuitous and I shall not advise it again.

A good example of such a coincidence occurred recently when a patient with renal failure of six days' duration due to lower nephron nephrosis passed about 100 c.c. of urine immediately before I had arranged to do a bilateral lumbar sympathetic block. It was therefore postponed, for a diuresis had commenced spontaneously; if I had arranged to do the block in the morning instead of the afternoon we might naturally have imagined that it was the cause of the diuresis.

#### *Recent Principles of Treatment*

*Phase I.*—I have made it a rule that in the assessment of these cases cystoscopy and catheterization of the ureters should be done as early as possible in every case in order to distinguish renal from post-renal cases, in other words, to exclude ureteric obstruction. This, I am sure, is of great importance. If obstruction is present, then unless it can be relieved easily by some simple procedure such as catheterization of the lower ends of the ureters to dislodge a plug of sulphonamide crystals, efforts should be directed towards draining the part of the urinary tract above the obstruction as a life-saving measure, rather than performing some definitive operation such as removal of a ureteric calculus or reimplantation of a ureter into the bladder. I do not believe that one should leave ureteric catheters indwelling for longer than six hours, there is a great danger that they may become blocked and thus themselves cause obstruction. If drainage is required for a longer period then I prefer to perform a nephrostomy.

Every effort is made to restore the circulating blood to as near a normal condition as possible, for haemoglobin levels are often surprisingly low. Even in the case of anuria due to mismatched transfusion, expert cross-matching will allow further blood to be given with advantage.

As soon as convenient a biochemical blood analysis should be done. This allows gross errors to be discovered and also sets a standard which enables one to assess any variations that may occur. The blood sodium, chloride, bicarbonate and urea tests are adequate in most cases.

*Phase II.*—The management of the second phase largely consists in catering for the reduced fluid requirements of the body, giving low protein and high carbohydrate diet, and watching the blood chemical results until the time comes to employ some method of artificial removal of waste products from the blood. I have no personal experience of external dialysis by any type of artificial kidney, and my impression is that it is not less complicated than methods of internal dialysis. The most effective of these is peritoneal dialysis, which was therefore chosen as being easier and safer. That it is neither easy nor safe I would hasten to assert, because it keeps a surgeon, a biochemist, and two nurses employed almost full time, and the electrolyte changes occur with such rapidity that it is extraordinarily easy to do more harm than good. But that it is a powerful therapeutic weapon we have no doubt whatever.

There are two types of case in which it seems desirable to employ dialysis. First it may be indicated in the patient in whom attempts to produce a diuresis have included the administration of excess of fluid with resultant œdema. If there is clinical pitting œdema present it is unlikely that restitution of the normal fluid levels will occur simply by limiting fluid intake by mouth over a period of a few days, and in any case it is necessary to restore the blood values to normal as soon as possible if prolongation of the necessary recovery period is to be avoided. The following is an example of this:

| G. D., AGED 40 YEARS. ANURIA 5 DAYS |          |               |                 |                   |                    |               |
|-------------------------------------|----------|---------------|-----------------|-------------------|--------------------|---------------|
| Day                                 | Hb.<br>% | Proteins<br>% | Sodium<br>mg. % | Chloride<br>mg. % | Bicarb.<br>vols. % | Urea<br>mg. % |
| 5                                   | 27       | 5.0           | 305             | 490               | 45                 | 188           |
| 7                                   | 32       | 6.0           | 315             |                   |                    | 225           |
| 9                                   |          |               | 330             | 450               | 55                 | 204           |
| 11                                  | 46       | 6.0           |                 |                   |                    | 177           |
| 13                                  | 68       |               |                 | 495               | 68                 | 171           |
| 15                                  |          |               |                 |                   |                    | 186           |
| 17                                  |          |               |                 |                   |                    | 282           |
| 19                                  |          |               |                 |                   |                    | 321           |

} Peritoneal  
dialysis

This patient had renal cortical necrosis resulting from an accidental hæmorrhage associated with Rhesus sensitization, and had received fluids in large amounts so that after five days of renal failure she had generalized œdema. Great clinical improvement occurred in the first forty-eight hours of dialysis, and the œdema became negligible. Recovery of the kidneys did not occur, however, and dialysis was discontinued on the 14th day; the patient died on the twenty-eighth day after the onset of renal failure.

The second type of case is that in which the second phase is prolonged and renal function does not return, so that the patient is in danger of death from accumulation of metabolic products. Here dialysis is used simply to prolong life so that the kidneys may have a greater chance of recovery as in the following case:

| F. S., AGED 60 YEARS. OLIGURIA FOR 4 DAYS |               |                 |                   |                    |               |
|-------------------------------------------|---------------|-----------------|-------------------|--------------------|---------------|
| Day                                       | Proteins<br>% | Sodium<br>mg. % | Chloride<br>mg. % | Bicarb.<br>vols. % | Urea<br>mg. % |
| 5                                         | 6.3           | 306             | 530               | 42                 | 436           |
| 6                                         | 6.2           | 314             | 500               | 58                 | 502           |
| 7                                         |               |                 |                   |                    | 500           |
| 8                                         | 6.2           | 318             | 530               | 44                 | 475           |
| 9                                         | 5.9           |                 |                   | 47                 | 500           |

} Peritoneal  
dialysis

This was a case of calculus anuria; secretion of urine started again but he developed auricular fibrillation and died of cerebral thrombosis.

The indications in these types of case for the use of dialysis are of course not as yet finally decided, but it has seemed that in the first variety the presence of generalized œdema is sufficient indication. A blood dilution which has not reached the stage of gross œdema can be dealt with by simple limitation of fluid intake for one or two days, but anything more demands quicker and more effective methods. In the second type we watch the blood urea value climbing day by day, with singularly little change in the clinical condition of the patient, and any decision to use dialysis must be made on the results of blood analysis alone, because death when it occurs may be very sudden.

I have been greatly impressed by the effect of dialysis upon the electrolyte content of the blood, changes occur rapidly and it is possible to restore a patient to an almost normal condition within a period of twenty-four hours; but it has not been possible to remove sufficient urea to reduce the blood level to normal or anywhere near it. It has seemed that the former function is often as important, if not more important, than the removal of urea.



It has been found that a blood urea level of 200 mg. % in the presence of little or no excretion by the kidneys represents a level beyond which delay is dangerous. This is the present basis of our treatment of these cases, though I would emphasize that with greater experience I may alter my ideas.

**Phase III.**—We now come to the third phase, or the period of diuresis. The main thing about this period is that although urine is being produced again, with the resultant vast increase in morale both of patient and nursing staff, the patient is by no means out of danger, and the strictest supervision of fluid and salt intake must continue if sudden death is to be avoided. As we know, the first urine that is passed is simply a glomerular filtrate, and this appears in larger and larger quantities, so that much fluid may be lost and the patient passes fairly rapidly from one condition in which the fluid intake must be limited to another in which the intake must be controlled by the amount that is excreted. The volume may be enormous, but fortunately the patient feels thirsty so drinking is easy. This fluid loss carries with it in solution sodium chloride in large quantities because tubular reabsorption of this salt is inadequate, and this may have dangerous results. It is possible by measuring the chloride content and the daily volume of the urine to work out exactly how much salt is needed to replace that lost, and this may be given by mouth or intravenously. As a rough guide we have found that half the daily total fluid excretion replaced as normal saline by mouth should cover the amount lost and can be taken by the patient.

The figures from a successful example of this three-phase management are given below:

| Day | Hb.<br>% | Proteins<br>% | SULPHONAMIDE NEPHROSIS |                   |                    | Urea<br>mg. % | Fluid intake<br>ml. | Urine<br>ml. |
|-----|----------|---------------|------------------------|-------------------|--------------------|---------------|---------------------|--------------|
|     |          |               | Sodium<br>mg. %        | Chloride<br>mg. % | Bicarb.<br>vols. % |               |                     |              |
| 2   | 82       | 6.3           |                        |                   |                    | 48            | 3,000               | 50           |
| 4   |          |               | 298                    | 500               | 56                 | 100           | 1,500               | —            |
| 6   | 72       | 6.3           | 308                    | 515               | 55                 | 140           | 900                 | 170          |
| 8   | 68       |               |                        |                   |                    | 197           | 2,000               | 1,440        |
| 10  | 68       | 6.3           | 328                    | 627               | 50                 |               | 3,210               | 3,210        |
| 12  | 68       |               |                        |                   |                    | 190           | 3,330               | 2,670        |
| 14  |          | 7.9           | 319                    | 605               |                    | 156           | 6,120               | 6,000        |
| 16  | 73       |               |                        |                   |                    |               | 5,800               | 5,000        |
| 18  |          | 6.9           | 322                    | 580               | 57                 | 62            | 7,260               | 7,590        |
| 20  | 68       |               |                        |                   |                    |               | 10,700              | 9,720        |
| 22  |          |               |                        | 605               |                    | 30            | 6,760               | 6,000        |

This was a woman aged 28, who, when 7½ months pregnant, developed lobar pneumonia. She was given in error a double dose of sulphathiazole, having 60 grammes in four days, and the next day she developed hæmaturia followed by complete anuria. She was seen on the second day of anuria and limitation of fluids commenced. Cystoscopy and catheterization of the ureters demonstrated no obstruction and no urine secretion. After the first blood analysis the fluid intake was reduced to less than one litre daily for two days with resultant improvement in the figures on the sixth day; on this day a medical induction produced a normal labour and a living child. Urine production commenced shortly before labour, and a diuresis was well under way by the tenth day. On the twentieth day she produced nearly 10 litres of urine and took by mouth 5 litres of normal saline and over 5 litres of other fluid.

#### Phase I MANAGEMENT OF PATIENT WITH ANURIA: SUMMARY

- (1) Remove cause; restore blood volume, blood-pressure and hæmoglobin level by transfusion.
- (2) Cystoscope and catheterize both ureters; if obstruction is found, relieve it or perform nephrostomy.
- (3) Estimate blood sodium, chloride, bicarbonate and urea.

#### Phase II

- (1) Limit fluid intake to make up for insensible loss.
- (2) Maintain adequate hæmoglobin level by transfusion (packed cells are useful).
- (3) Give low protein, high carbohydrate, diet.
- (4) Check progress by estimating blood urea and bicarbonate on alternate days, at least.
- (5) Employ dialysis if generalized œdema is present, or blood urea has risen to 200 mg. %.

#### Phase III

- (1) Replace fluid excreted.
- (2) Replace salt excreted.
- (3) Check progress by estimating blood sodium, chloride, bicarbonate and urea every two to three days until diuresis subsides.

#### REFERENCES

- COLLER, F. A., *et al.* (1948) *Ann. Surg.*, **128**, 379.  
 DARMADY, E. M. (1948) *Proc. R. Soc. Med.*, **41**, 418.  
 LATTIMER, J. K. (1945) *J. Urol.*, **54**, 312.  
 LUCKÉ, B. (1946) *Milit. Surg.*, **99**, 371.  
 MUIRHEAD, E. E., *et al.* (1948) *Blood*, **3**, 101.  
 REID, R. W. (1948) *Proc. R. Soc. Med.*, **41**, 413.

## Observations on Familial Polycystic Disease of the Kidney

By J. D. FERGUSSON, M.D., F.R.C.S.

*Central Middlesex Hospital*

POLYCYSTIC disease of the kidney has been described as a disease of paradox, manifesting itself typically in the newborn and middle-aged, and lying concealed in childhood. At one extreme it may present the obstetrician with a novel aspect of urology, and at the other, the physician with a tangible cause for hypertension. To the urologist the widespread supplanting of functional renal tissue by cysts, in surviving cases, acts as a reminder of the enormous margin of excretory safety provided by the kidney. It is, in fact, this multiplicity of cysts of various sizes, developing so as to distort the pelvis and increase the bulk of the renal mass, which distinguishes the condition from other cystic affections of the kidney.

Among the earliest descriptions of the disease is that of Littré from Paris in the year 1700, followed closely by Heer, also from France, and Osiander from Germany. Increasing numbers of cases have since been published and recognition of the condition is now so universal as to make case-reports superfluous unless forming part of a series, or complicated by some peculiarity. From recorded series of cases, however, we can obtain some idea of the incidence of the disease, as shown in the following table:

### POLYCYSTIC DISEASE OF THE KIDNEY INCIDENCE

#### Cases admitted to hospital:

|            |                                           |
|------------|-------------------------------------------|
| 1 in 5,000 | — Cairns, London Hospital.                |
| 1 in 3,523 | — Braasch and Schacht, Mayo Clinic.       |
| 1 in 3,500 | — Oppenheimer, Mount Sinai Hospital, N.Y. |

#### Cases found at autopsy:

|            |                                                      |
|------------|------------------------------------------------------|
| 1 in 1,019 | — Braasch and Schacht, Mayo Clinic.                  |
| 1 in 600   | — Preitz, Kiel.                                      |
| 1 in 428   | — Oppenheimer, New York.                             |
| 1 in 250   | — Sokoloff, Leningrad.                               |
| 1 in 242   | — Garceau, Boston.                                   |
| 1 in 158   | — Jewish Hospital Brooklyn. (Quoted by Oppenheimer.) |

1 in 356 — (In a collected series of 23,900 autopsies) Davis.

My own series of 29 cases, occurring among just over 100,000 hospital admissions, falls closely into line, showing a ratio of 1 case in 3,500 admissions, and an autopsy incidence of 1 in 375. 16 of the cases have been confirmed at post-mortem, while in the others a combination of clinical and pyelographic findings leaves no reasonable doubt as to the existence of polycystic disease.

From the table it will be seen that clinical recognition is somewhat at variance with the post-mortem findings. This brings out an important point implying that only 1 in approximately 10 cases is diagnosed before death. The explanation lies no doubt partly in the fact that while some cases remain symptomless, others in whom the disease may be suspected cannot be confirmed until autopsy.

It will be further noted that the disease is universal in distribution, and, from clinical and autopsy figures, an average of from 2 to 3 cases should occur in the practice of a large hospital in the course of each year.

The observations contained in this paper are based on a study of the 29 subjects already referred to and on a review of the literature dealing with familial cases, and concern certain aspects which have interested me in connexion with the hereditary tendency of the disease.

Although clearly recognized, the familial tendency of polycystic renal disease is one which, apart from comprehensive studies by Bunting (1906) and Cairns (1925), and reports by Thompson (1903) and Fuller (1929), has received comparatively little attention in this country. From a wider survey of the literature, however, it is clear that such an incidence is well established, and the number of familial instances recorded bears a high ratio to the individual cases described.

The earliest suggestion that the disease might be inherited is probably attributable to Adamkiewicz in 1843, although by mistranslation Schupmann is sometimes credited a year earlier. At the beginning of the present century Dunger (1904) was able to compile a list of twelve families, while in 1924 Maier recorded twenty-five familial instances out of a total of 300 recorded cases. It is probable that some of these earlier reports should be treated circumspectly since diagnosis rested mainly on clinical findings and was not invariably substantiated by pyelographic or autopsy records. In 1925 Cairns published his investigation of a family at the London Hospital in which 10 members were affected in three generations, and appended an authoritative review of 23 familial reports available to him at that time. Up till

then the disease had not been traced for more than two generations, except in Crawford's record (1923) of probable, though unproven, cases in four generations, and in a family described by Bull (1910) to which a third generation case was added by Paus (1914). In 1929 Fuller added a further instance of affection through four generations, and since that time numbers have increased to the extent that by 1940 Werner had collected 109 families including over 350 affected members:—

WERNER (quoted by Savera)

109 Families (over 350 individuals).

40 observations in one generation.

41 observations in two generations.

8 observations in three generations.

3 observations in four generations.

17 unstated.

From other sources and a personal investigation of six families I have accumulated details of 84 families with 307 examples of the disease.

One cannot help being somewhat amused by certain characteristic touches in the familial case-histories from foreign parts—a hausspielerin, or dancer, with her father from a Berlin music-hall, several instances of pregnancy bringing the condition to light in Paris, and automobile accidents in the States accounting for ruptured cystic kidneys, to say nothing of the opportunity afforded by the large families of those of more catholic taste.

My interest in the familial tendency of the disease was first aroused by two sisters and a brother, all suffering from the disease, who consulted me independently within the course of a few months. Each had experienced recurrent attacks of pyelitis and presented easily felt bilateral nodular renal masses. The pyelographic appearances were typical in every instance. From subsequent enquiry and examination it transpired that 2 further sisters were similarly affected giving a total of 5 siblings with the disease in a generation of 12 members.

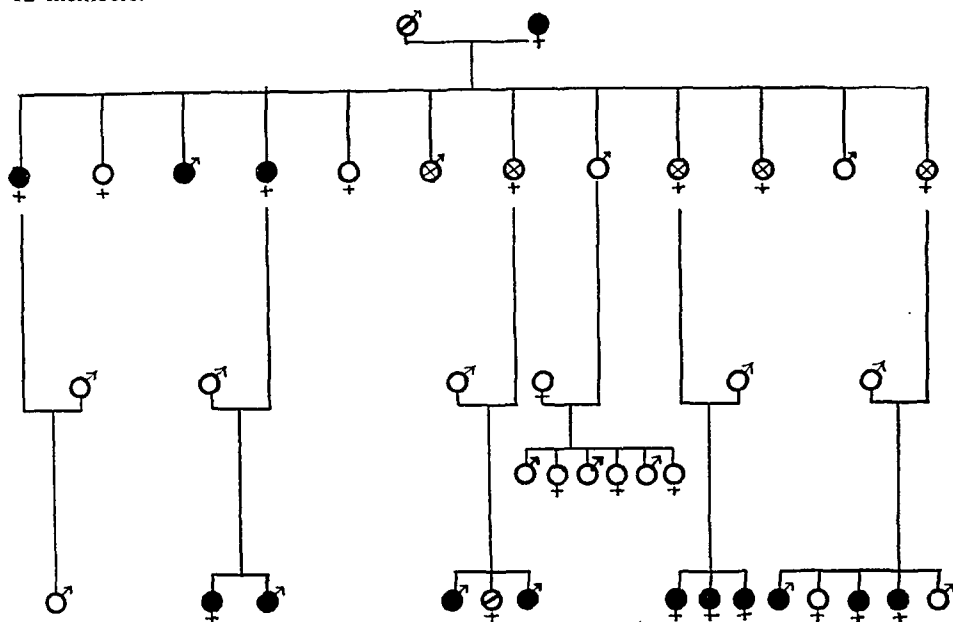


FIG. 1.

FIGS. 1-6.—Explanation of symbols:

⊗ Proved polycystic renal disease.

● No evidence of disease clinically or pyelographically.

⊙ Suspicious, though unproven.

○ Not examined.

FIG. 1 shows the distribution of cases in this Irish family. The ages of the affected individuals (cross in circle) range between 37 and 47 years and the sex incidence is predominantly female. For reasons referred to later 14 additional members of the family were examined without finding a further proven case. These are indicated by solid black circles (with the exception of one individual with albuminuria and a suspicious pyelogram shown with a bar in circle). The father of the first generation (also shown by a bar) was said to have died from

uræmia with enlarged kidneys at the age of 47. His wife at the age of 70 presents no evidence of the disease and shows normal pyelographic appearances. There is, therefore, strong presumptive evidence that the father transmitted the disease.

My further experience of the disease has indicated that whenever other members of the family are available for investigation a strong familial tendency can nearly always be established. This may be of distinct value from the diagnostic, and probably also from the prognostic, point of view. Thus, after excluding the 5 cases in my first family, 13 of the remaining 24 cases could be grouped in 5 unrelated families, while the residual 11 consisted of solitary individuals with no accessible relatives, and 3 neonatal cases in first-born children. Further reference will be made to these later. The distribution of the 13 additional familial cases is shown briefly in the following figures.

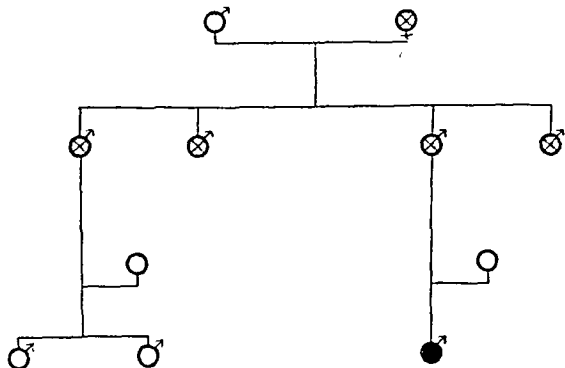


FIG. 2.

FIG. 2.—A family including 4 brothers and their mother, 3 proved at post-mortem, and 2 established by clinical examination and pyelography. All had enormous kidneys (weighing 7 lb. each at autopsy), and all 4 brothers had hypertension. The mother died at the age of 56, while the disease was detected in the brothers at ages ranging between 31 and 41. 3 are now dead of apoplexy and uræmia, and one was surviving three years ago with marked hypertension. In this family the distribution is predominantly male, but the transmitting sex appears to be female. One further member of the family was investigated with negative results.

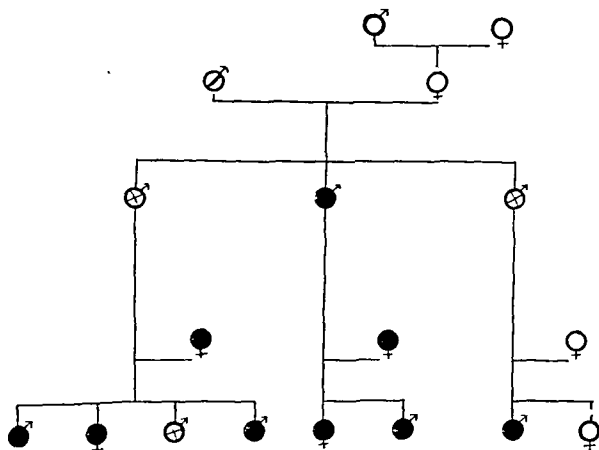


FIG. 3.

FIG. 3.—A family including a father and son and the father's brother, which is unique among my families in showing one adult and a young child in the same family. The boy was operated on elsewhere for a renal tumour at the age of 5, but after exposure of a polycystic right kidney the wound was closed. Pyelography has since shown the disease to be bilateral. The father, aged 48, has palpable kidneys and a positive pyelogram and suffers from recurrent pyelitis. The father's brother died recently from pneumonia at the age of 49 and bilateral polycystic kidneys were found at post-mortem. The grandfather (shown by a bar

in circle) died of renal disease at an early age. The sex incidence is entirely male, and the transmission also male as the boy's mother is negative both clinically and radiographically. No additional cases were found in 8 further members of the family who were investigated.

The remaining 3 families contain only 2 proven cases each, though in many cases other members are regarded as suspicious.

FIG. 4.—A family including a mother and daughter, both of whom died of uræmia aged 46 and 33 respectively, and were confirmed at post-mortem as having bilateral polycystic kidneys. The history of the mother's generation is interesting in that no fewer than 3 brothers

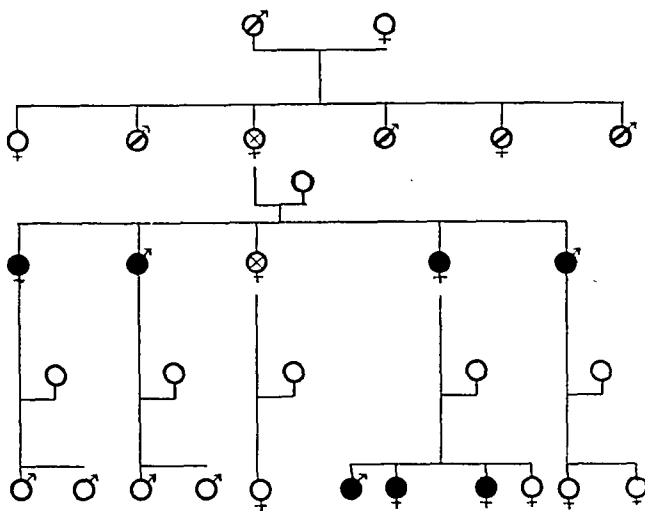


FIG. 4.

and a sister were said to have died of renal disease at ages varying between 40 and 50. 7 additional members of later generations were examined without a further case coming to light.

FIG. 5.—A family including 2 sisters aged 37 and 58. The former died of pulmonary tuberculosis and was found to have bilateral polycystic disease at post-mortem. The older case was first diagnosed at the age of 50 when she had a nephrectomy elsewhere for hæmaturia.

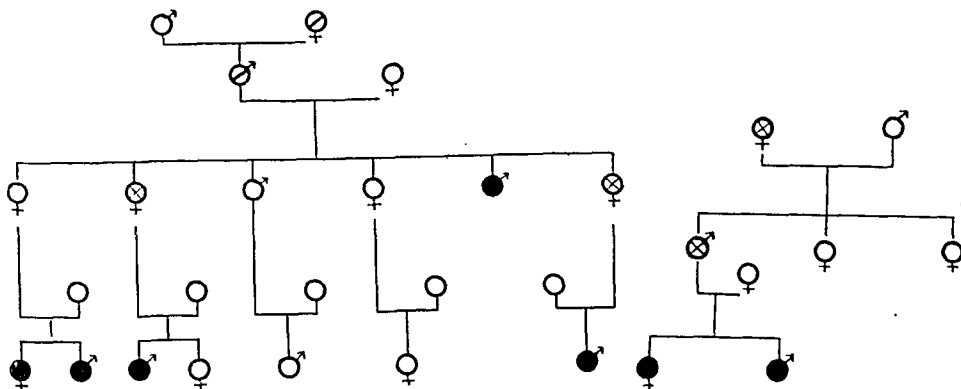


FIG. 5.

FIG. 6.

She was subsequently blown out of her room during an air-raid and suffered a severe bout of hæmaturia from the remaining kidney, but survived a further four years till her death from uræmia in 1948. The remaining kidney was polycystic at autopsy. The father and grandmother died of renal disease, but no trace of the condition could be found in 5 other members of the family who were investigated.

FIG. 6.—A family including a mother and son. The mother died of uræmia aged 48, with bilateral polycystic kidneys confirmed at autopsy. The son has bilateral renal masses and positive pyelographic findings at the age of 32. His 2 children have been investigated with negative results.

My object in demonstrating these families and reviewing the literature in familial cases is to stress the opportunity available for genetic study, and to point out certain features which emerge from their consideration.

In the first place it is clear that familial records can be divided into two groups depending on whether several generations are affected or whether all the cases are siblings (that is brothers and sisters). In the former group we obviously have the opportunity in many cases of determining the sex of the transmitting individual, while in all cases we are able to obtain a record of the sex incidence. Some authors, among them Thomson-Walker (1914) and Marion (1935) have stated that female cases preponderate, but most are agreed that the transmitting sexes are evenly divided. On analysing the 84 families to which I have alluded, both sex incidence and transmitting incidence appear about equal within the standard variation.

| 84 FAMILIES (307 INDIVIDUALS) |    |    |    |     |
|-------------------------------|----|----|----|-----|
| <i>Sex Incidence</i>          |    |    |    |     |
| Males                         | .. | .. | .. | 132 |
| Females                       | .. | .. | .. | 115 |
| Unstated                      | .. | .. | .. | 60  |
| <i>Transmitting Sex</i>       |    |    |    |     |
| Male                          | .. | .. | .. | 35  |
| Female                        | .. | .. | .. | 33  |

In families showing more than one affected generation there appears no doubt that, where possible to trace, the disease is inherited on the lines of Mendelian dominance.

We next come to the age of the affected individuals at the time of recognition of the disease, and in this connexion, owing to the inadequacy of many records, I am unable to give a comprehensive account. As far as my own individual cases and families are concerned the findings are shown in fig. 7 A and B.

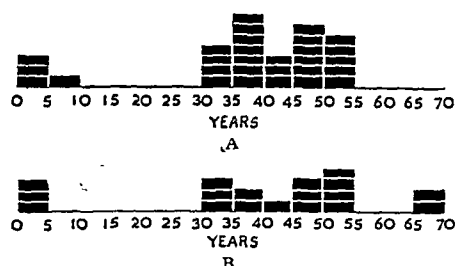


FIG. 7.—Polycystic disease of the kidneys.  
A.—Age at time of diagnosis in 29 cases.  
B.—Age at death in 18 cases.

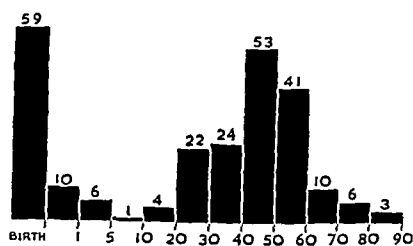


FIG. 8.—Polycystic disease of the kidneys.  
Age incidence in 239 cases (Küster).

These conform to the generally accepted view that the disease has two peaks of incidence, one between 30 and 50 years of age, and the other denoting neonatal cases. This fact puzzled Virchow (1856) who put forward his theory of intra-uterine renal papillitis to account for the neonatal cases, and also remarked their frequent association with other congenital abnormalities of the urinary tract.

Küster, about 1900, showed the two peaks of incidence very clearly in a study of 239 collected cases (fig. 8). Among these 59 were dead at or shortly after birth, and 10 died in the first year, while only 11 further cases were found below the age of 20. There has, in fact, always been a paucity of recorded cases in children and young adults which is very difficult to explain and which has even led to the view that the neonatal and adult diseases might be distinct. Sieber (1905) was able to find 28 examples of the disease in childhood out of 212 cases and Meredith Campbell's series (1937) of 48 children contains only 6 over the age of 1. Through the courtesy of the Honorary Staff at the Hospital for Sick Children, Great Ormond Street, I have also been able to confirm the remarkably low incidence among their cases.

Now, this is clearly a problem which should be examined in the light of familial records of the disease, and particularly since affected parents are apt to enquire as to the potential liabilities of their fecundity. The issues to be determined are as follows:

- (1) What are the chances of neonatal cases occurring in a family of affected adults?
- (2) If the disease, as it appears apt to do, remains latent in childhood, are there any means by which prospective cases can be determined before becoming full-blown?
- (3) Are there any new grounds for disputing the affinity of neonatal and adult cases?

I will deal briefly with these questions in order.

(1) In the 84 families which I have reviewed neonatal cases are recorded in 8. In none of these families were there any examples of the adult disease. In other words, although there are records of 307 affected individuals in these families there is no proved reference to the occurrence of the adult and neonatal forms of the disease in an individual family. A suspicion attaches to one family, quoted by Höhne (1896), in which a mother and grown-up daughter were affected, and a further child died of renal disease at 9 weeks, but this infant case, however, was never proved. All the neonatal familial cases then have occurred in siblings, and in no instance has an affected parent been recorded with certainty.

It seems to follow then that although affected parents are unlikely to produce neonatal cases, families in which newborn cases have already occurred are prone to further affliction. In such cases the parents exhibit no evidence of the disease, and the method of hereditary transmission is open to argument.

Among my own 29 cases there were 3 babies stillborn with the disease. In 2 instances where it was possible to investigate both the parents (who incidentally were unrelated) no clinical or pyelographic evidence of the disease could be proved.

(2) The recognition of latent cases in childhood is an aspect of the disease which I have found particularly interesting. Even though little could probably be done if a case were established, it is understandable that the resolution of that element of doubt present in every affected parent's mind would be welcomed—more especially if it could be shown that a particular child would never be affected.

It occurred to me that if it were possible to establish a linkage between the disease and any recognizable genetic factor, the latter might serve to unmask the dormant condition. It will be remembered that in the family investigated by Cairns several of the members were affected by a form of inherited myopia, but this did not appear to be linked to the disease. The underlying idea is, of course, similar to that in current vogue in breeding sex-linked poultry and livestock, but unfortunately the number of known genetic factors in man is still somewhat small. Recognizable genetic factors include the standard blood groups with the addition of the M, N, P and Rh factors, ability to taste phenylthiocarbamide and to secrete haptenes in the saliva, as well as a number of physical peculiarities exemplified by hair and eye colour, hyperextensibility of phalanges, attachment of ear lobes, &c. Accordingly, in 5 of my families a variety of these tests, in conjunction with clinical and pyelographic examination, was applied to all available members both affected and unaffected. Figs. 9 and 10 illustrate some of the results in 2 of the families. I have limited the list of genetic factors to blood grouping and typing, salivary secretion of haptenes, and ability to taste P.T.C., on account of available space. In the majority of cases a careful survey of the physical factors was also carried out. In each case the *blood grouping* is indicated on the first line of lettering, *salivary secretion* by the letter "S" (plus or minus) on the second, and *Phenylthiocarbamide tasting* by the letter "T" (plus or minus) on the third. It will be noted, however, that none of the specific serological or biochemical factors appears to be linked to the disease, and this applies also to the physical factors which I have omitted.

In all, over 50 individuals were examined in this way, but despite a considerable amount of work and some difficulty in tracing relatives, no linked genetic factor could be determined.

Although disappointing I do not regard this as labour in vain, I feel the air has been cleared to some extent, and I hope that with the identification of new genetic factors a linkage may ultimately be found.

Before concluding these observations on the detection of latent cases in childhood I would mention that I have followed up several children of affected parents by annual intravenous pyelography, and in no instance have the appearances become suspicious of developing disease. So far as I am aware no child with a negative pyelogram has yet been shown to become positive later. This is an important point since it may imply that the latent disease is usually demonstrable pyelographically, in which case there is little need for further genetic research in this respect.

(3) Finally, I would like briefly to review the affinity of the neonatal and adult forms of the disease in the light of my inquiries. It has been generally agreed in later years that both form examples of the same disease, founded on a theory of maldevelopment initiated by Hildebrandt (1894) and elaborated by Kampmaier (1923). Before unreservedly accepting this assumption, however, the following points seem worthy of consideration:

(a) The age incidence of the disease shows a remarkable peculiarity in having two widely separated peaks at birth and middle-age respectively. Although cases undoubtedly occur in childhood they are hardly sufficiently numerous to fill the gap.

(b) Investigation of family records reveals no proved case of the adult and neonatal cases occurring in the same family.

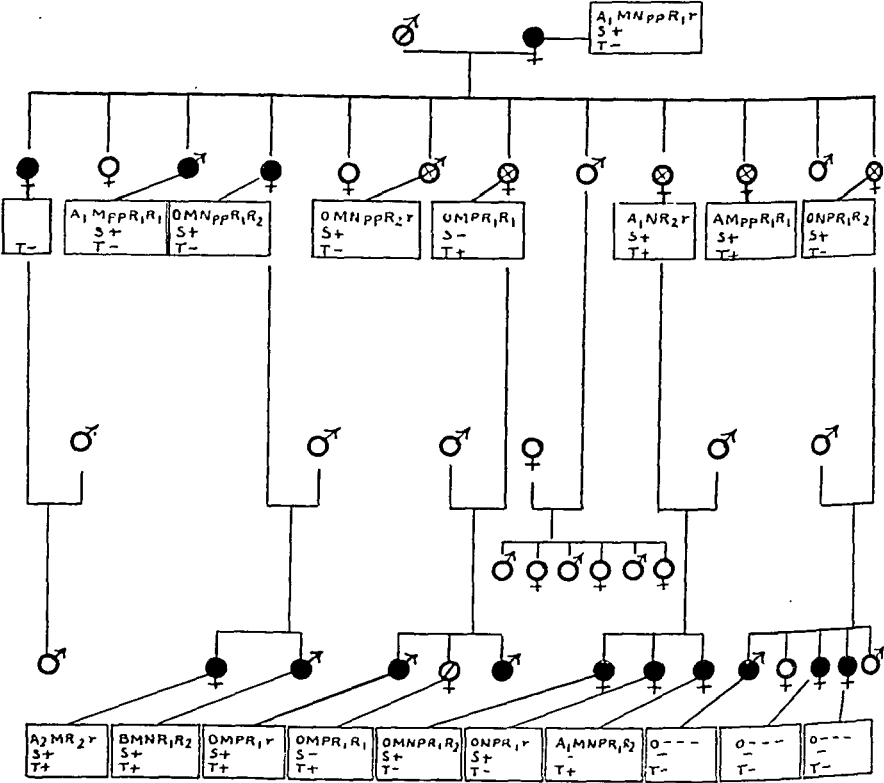


FIG. 9.

FIGS. 9 and 10.—Distribution of genetic factors in families showing polycystic renal disease. First line: Blood groups and types. Second line: Salivary secretion; ( ) haptenes (S+ or S-). Third line: Ability to taste phenylthiocarbamide (T+ or T-).

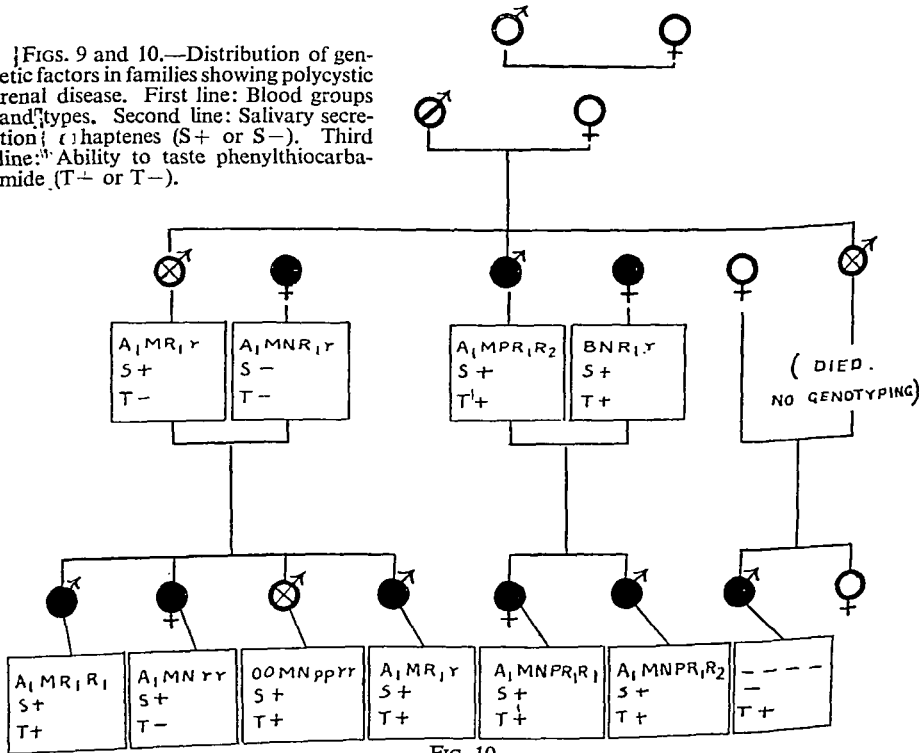


FIG. 10.



(c) Although the adult disease appears to be inherited on the lines of Mendelian dominance, parents of neonatal cases have shown no evidence of disease pyelographically or clinically. This would indicate that the neonatal condition was inherited as a recessive rather than as an irregular dominant characteristic.

(d) Although associated with stillbirth or early demise, the kidneys of affected neonatal cases are often not enlarged to an extent comparable with surviving adult cases, and the cysts are commonly smaller and more uniform in size.

(e) Association with other abnormalities of the urinary tract such as ureteric stricture and vascular anomalies is common in neonatal cases. In Campbell's 48 children ureteric obstruction was present in 7, and 12 others exhibited urogenital anomalies. Such peculiarities are seldom seen in the adult, but, of course, many of them would doubtless preclude survival.

(f) Histologically it has been suggested by Lambert of Brussels (1947) that, after reconstruction of serial sections, it may be possible to trace a connexion between cysts and collecting ducts in the adult, but not in newborn cases. The position and function of the cysts also appear to vary according to the status of the case. (Despite these discrepancies the author appears to favour a monistic aetiology for the disease.)

Now these observations are open to criticism, and it appears that three possibilities exist. Either newborn and adult cases have a common aetiology, or they are different diseases. Or, thirdly, as a compromise, some neonatal and childhood cases have a common origin with the adult form, while the remainder (mainly atypical) result from other developmental mistakes.

This last supposition would appear to be supported by the recent case-reports of Howze and Hill (1949) in which a number of unilateral polycystic kidneys in children were found to be associated with gross vascular anomalies. The previous work of Hepler (1930) on the production of cystic kidneys by experimental interference with the blood supply also falls into line with this. I feel, therefore, that on the evidence I have adduced there may be some grounds for separating the neonatal disease into two groups, and would make a plea for more careful observation of this condition.

To sum up, I have referred to the incidence of polycystic renal disease in hospital practice, and the high ratio of familial cases. Analysis of these cases has shown an equal distribution between the sexes, both affected and transmitting, but indicated a distinction between adult and neonatal forms which may have some prognostic significance.

Emphasis has been laid on the apparent rarity of the condition in children, and the difficulty of anticipating the later development of the disease. In this connexion reference has been made to an investigation with the object of determining a linkage between the disease and a common genetic factor whereby the condition, if dormant, could be recognized in childhood. Unfortunately no linkage could be established, but this does not preclude the possibility of success when further genetic factors become known. I have also alluded to the absence of pyelographic records of developing disease, and have adduced evidence from my observations to indicate that a common aetiology for all forms of the disease is not fully established.

I should like to acknowledge my indebtedness to Professor L. Penrose of the Galton Laboratory for the help he has given me in the genetic investigation of my cases, to Dr. G. Discombe for his valued collaboration in the blood grouping, and also to Miss D. M. Barber and her assistant for the preparation of the diagrams which have illustrated this communication.

#### BIBLIOGRAPHY

(All references to familial cases are marked with an asterisk)

- ADAMKIEWICZ (quoted by Bunting, 1906).
- ALBRITTAI, J. W., and CORNBROOKS, E. I. (1939) *Bull. Sch. Med. Univ. Maryland*, 24, 121.
- \*BAR (quoted by Bunting, 1906).
- \*BECK, C. (1901) *Ann. Surg.*, 33, 147.
- BOINET, E., and RAYBAUD, A. (1903) *Rev. Méd. (Paris)*, 23, 1.
- \*BORELIUS, J. (1901) *Nord. med. Ark.*, 34, 1.
- \*BRAASCH, W. F., and SCHACHT, F. W. (1932) *Trans. Amer. Ass. Gen.-urin. Surg.*, 25, 71.
- \*BRÜCKNER, C. (1869) *Virchows Arch.*, 46, 503.
- \*BULL, P. (1910) *Norsk Mag. Laegevidensk.*, 8, 808.
- \*BUNTING, C. H. (1906) *J. Exper. Med.*, 8, 271.
- \*BURGER (quoted by Maier, 1924).
- \*CAIRNS, H. W. B. (1925) *Quart. J. Med.*, 72, 359.
- CAMPBELL, M. F. (1937) *Pediatric Urology*. New York, 1, 202.
- \*CANNON, J. F. (1947) *Ann. Int. Med.*, 27, 610.
- \*CARBONNEL (quoted by Couvelaire, 1899).
- \*CARREZ (quoted by Bunting, 1906).
- COUVELAIRE, A. (1899) *Ann. gynec. obstet.*, 52, 453.
- \*CRAWFORD, R. H. (1923) *Surg. Gynec. Obstet.*, 36, 185.
- \*CUMMING, R. E. (1928) *J. Urol.*, 19, 149.

- DAVIS, J. E. (1925) *Amer. J. Obstet. Gynec.*, 9, 758.
- \*DUNGER, R. (1904) *Beitr. path. Anat.*, 35, 445.
- \*EISSENDRAETH, D. N. (1919) *Surg. Clin. Chicago*, 3, 1057.
- \*FARR (quoted by Maier, 1924).
- \*FLINTERMANN (quoted by Maier, 1924).
- \*FORT, A. (1941) *An. Cir.*, 7, 199.
- \*FULLER, C. J. (1929) *Quart. J. Med.*, 22, 567.
- \*FUSS, E. M. (1933) *Z. Urol.*, 27, 317.
- GARCEAU (quoted by Crawford, 1923).
- \*GAYET and BANSILLON (1922) *Lyon méd.*, 131, 771.
- \*GEISINGER, J. F. (1935) *J. Urol.*, 34, 202.
- \*GOLDSTEIN, A. E. (1935) *J. Urol.*, 34, 509.
- \*GORDON, G. R., and TRASOFF, A. (1937) *Amer. J. med. Sci.*, 194, 112.
- \*GOTTLIEB, J. G. (1925) *Z. urol. Chir.*, 17, 256.
- \*HALBERTSMA, T. (1931) *Z. Kinderheilk.*, 52, 145.
- \*HALTGREN (quoted by Maier, 1924).
- \*HAUSMAN, H. (1940) *Amer. J. Surg.*, 49, 335.
- HEER, O. (quoted by Boinet and Raybaud, 1903).
- HEPLER, A. B. (1930) *Surg. Gynec. Obstet.*, 50, 668.
- \*HERNÁNDEZ, I. M., and DAMIANOVICH, J. (quoted by Fort).
- HILDEBRANDT (1894) *Arch. klin. Chir.*, 48, 343.
- \*HÖHNE, E. (1896) *Dtsch. med. Wschr.*, 22, 757.
- HOWZE, C. P., and HILL, J. H. (1949) *J. Urol.*, 61, 187.
- JACOB, P., and DAVIDSOHN, C. (1900) *Charité-Ann.*, 25, 16.
- JAHIER, M. (1938) *Gynec. et Obstet.*, 37, 278.
- KAMPMAIER, O. F. (1923) *Surg. Gynec. Obstet.*, 36, 208.
- KÜSTER, E. (1898-1902) *Die Chirurgischen Krankheiten der Nieren*. Stuttgart, 512.
- LAMBERT, P. P. (1947) *Arch. Path.*, 44, 34.
- \*LAUENSTEIN (quoted by Jacob and Davidsohn, 1900).
- \*LIGHTWOOD, R., and LOOTS, G. H. (1932) *Proc. R. Soc. Med.*, 25, 1230.
- LITTRÉ, A. (quoted by Boinet and Raybaud, 1903).
- \*LOVE, J. K., and RICHMOND, A. (1902) *Glasg. med. J.*, 57, 32.
- \*LYNCH, K. D., and THOMPSON, R. F. (1935) *Urol. cutan. Rev.*, 39, 426.
- MAIER, O. (1924) *Arch. klin. Chir.*, 132, 226.
- MARION, G. (1935) *J. Pract. Paris*, 49, 497.
- \*MARQUARDT (quoted by Savera, 1946).
- \*MEYER, E. (1903) *Virchows Archiv.*, 173, 209.
- \*MORRIS (quoted by Bunting, 1906).
- \*NOLAN, L. E. (1945) *Urol. cutan. Rev.*, 49, 734.
- \*OPPENHEIMER, G. D. (1934) *Ann. Surg.*, 100, 1136.
- OSLANDER, J. (quoted by Oppenheimer, 1934).
- \*OSLER, W. (1902) *Amer. Med.*, 3, 951.
- \*PAUS, N. (1914) *Dtsch. Z. Chir.*, 130, 628.
- PREITZ (quoted by Crawford, 1923).
- \*REASON, C. H. (1938) *Canad. med. Ass. J.*, 29, 612.
- \*REAVES, J. U. (1942) *Sth. Surg.*, 11, 254.
- \*RUMPLE, O. (1921) *Arch. klin. Chir.*, 116, 344.
- SAVERA, O. (1946) *Wien. klin. Wschr.*, 58, 422.
- \*SCHOCH, H., and SCHWEIZER, A. (1937) *Schweiz. med. Wschr.*, 67, 652.
- \*SCHUPMANN (quoted by Bunting, 1906).
- \*SHAPIRO, I. J. (1929) *J. Urol.*, 21, 308.
- SIEBER, F. (1905) *Dtsch. Ztschr. Chir.*, 79, 406.
- \*SIMMONDS (quoted by Maier, 1924).
- \*SINGER (quoted by Bunting, 1906).
- SOKOLOFF (quoted by Jahier, 1938).
- \*SPRENT, J. (1924) *Med. J. Austr.* (i), 63.
- \*STEINER (1899) *Dtsch. med. Wschr.*, 25, 677.
- \*STOCKMAN (quoted by Maier, 1924).
- \*TANDLER (quoted by Maier, 1924).
- \*TEUSCHER, M. (quoted by Albrittain and Cornbrooks, 1939).
- \*THOMPSON, T. (1903) (quoted by Cairns, 1925).
- THOMSON-WALKER, J. (1914) *Genito-Urinary Surgery*. London, 208.
- \*THORINGTON, C. (1934) *J. med. Ass. Alabama*, 4, 218.
- VIRCHOW, R. (1856) *Gesamm. Abh. z. Wiss. Medicine, Frankfurt*, 864.
- \*WALTHER (quoted by Savera, 1946).
- WERNER, M. (1940) in JUST, G. (ed.) *Handbuch der Erbbiologie des Menschen*. Berlin, 4, II, 828.
- \*WOBUS, R. E. (1918) *Surg. Gynec. Obstet.*, 27, 423.
- \*WOLFF, W. (1867) *Berl. klin. Wschr.*, 4, 480.
- \*ZONDEK (quoted by Maier, 1924).

## Section of Odontology

President—Professor SHELDON FRIEL, M.Dent.Sc., Sc.D., F.D.S.

[February 28, 1949]

### The Sterilization of Carious Dentine

By J. L. HARDWICK, M.D.S.

(*University of Birmingham*)

#### THE OBJECTS OF THE RESEARCH

IN the present research an effort has been made to find a chemical germicide suitable for sterilizing the mechanically sound carious dentine of a vital tooth. If such a germicide exists, it would be possible to treat carious dentine by excising the mechanically unsound tissue and sterilizing the mechanically sound tissue. As a result, natural calcific barriers between infected tissues and the pulp would not be removed, thus lessening the pain of cavity preparation and the pulpal irritation due to mechanical and thermal stimuli caused by the cutting of the cavity. In addition, fresh dentinal tubules along which chemical irritants from unsuitable cavity linings and cements could subsequently diffuse would not be opened over the floor of the cavity.

A suitable germicide would have to be penetrating and non-toxic to the pulp even if applied to vital dentine. The object of the research was therefore: (1) To find the most successful agents for sterilizing carious dentine, not only on the cavity surface but throughout its depth. (2) To ascertain whether the more successful agents have any deleterious action on the pulp when applied to carious tissue or to sound vital dentine.

#### SOME PRELIMINARY INVESTIGATIONS PRIOR TO EVOLVING A STANDARDIZED TECHNIQUE

Some preliminary investigations before the commencement of the research on the main bacteriological problems showed that:

(1) The grinding of a surface through sound enamel or dentine with a large stone revolving at high speeds sterilized that surface owing to the heat generated by the cutting. Care must be taken to avoid carrying infected material from unsterilized parts of the tooth by allowing the stone to wobble during the grinding.

If such surfaces were ground continuously for periods longer than one or two seconds, caries under the cut surface might also be sterilized by the heat generated.

(2) A round rose-head burr, size 1, revolving at high speeds would sterilize the harder types of clinically carious dentine in an appreciable proportion of cases. A similar burr revolving very slowly in a reducing handpiece did not sterilize carious dentine.

(3) Carious dentine would invariably contain viable bacteria at the end of a twenty-four hour period if the freshly extracted teeth were placed in a moist chamber at blood heat. At room temperature, living bacteria would be found in the caries of teeth similarly treated in 70% of cases.

#### THE STANDARDIZED TECHNIQUE USED IN THE BACTERIOLOGICAL INVESTIGATION

Based on a knowledge of these facts, a standardized technique was evolved for the bacteriological investigations on the effect of various bactericidal agents applied to carious cavities. The conditions under which each experiment was performed were rigidly controlled.

(1) As soon as was conveniently possible after extraction, the tooth to be treated was washed in a jet of warm water at approximately blood heat. If the period before the examination was unduly long (e.g. an hour) the tooth was kept in an incubator but in no case was the period allowed to exceed three hours.

(2) The cavity was dried with cotton-wool, thus removing surface debris.

(3) The germicide was applied for a period of two minutes and then washed away with a further jet of warm water.

(a) In the case of zinc oxide and oil of cloves dressings, the dressing was applied for a period of approximately three hours before being removed. In most cavities, some carious tissue had to be removed to provide retention for the zinc oxide and oil of cloves dressing. (With no other germicide was any carious dentine removed at any stage.)

(b) In the case of copal ether varnish, the varnish was allowed to remain *in situ* until the investigation was completed, normally a period of two and a half to three hours.

(4) In approximately half the experiments with each germicide the bacterial cultures were inoculated in a period from ten minutes to thirty minutes after the application of the germicide. These were called early tests. In the remaining experiments with each germicide, the bacterial cultures were inoculated in a period of from two and a half to three hours after the application of the germicide. These were called late tests. In the period subsequent to the application of the germicidal agent, the teeth were placed in an incubator.

The cultures were obtained as follows:

(1) The tooth was again washed under warm water, leaving the cavity moist. A surface was ground through the sound enamel and dentine with a large stone on a fast rotating lathe or dental engine. The tooth was applied intermittently to the stone for short periods of about one second. A surface was thus cut down to the sound dentine. Then, without contaminating the sterilized surface, a few grindings were taken from this surface with a sterilized No. 1 size rose-head burr in a slowly rotating handpiece and inoculated into glucose broth. This acted as a control for the sterilization of the cut surface.

(2) With the same burr a cavity was cut from the sterilized surface nearly through to the surface of the carious dentine, taking care to avoid the pulp cavity. The reducing handpiece was used as before and great care had to be taken in the later stages to avoid penetrating through the last layers of caries and thus reaching the surface. The grindings were inoculated into tubes of glucose broth and of 1% gelatine broth.

(3) The broths were incubated for periods of up to one week. Subculturing and microscopic examinations were performed as necessary to decide the types of organisms found.

The examination of the bacterial cultures was performed in the earlier periods of the research by Dr. J. Abbiss of Dalhousie University, Canada, who was then in the Bacteriological Department of the University of Birmingham, and in the later periods by his successor, Mr. F. W. Moore. The entire credit for the method of culturing the organisms and the examination of the cultures is due to them. The selection of glucose broth and 1% gelatine broth as the standard media was made by Mr. Moore.

#### THE BACTERICIDAL INDEX

In the course of these investigations over 1,000 tests were performed, involving the taking of over 3,000 bacterial cultures.

Three cultures were obtained for each test:

Culture A in glucose broth from the sterilized surface.

Culture B in glucose broth from the treated caries.

Culture C in 1% gelatine broth from the treated caries.

A positive result in Culture A from any experiment, of course, denoted an error in technique and therefore the test was discarded.

There is no justification for assuming in all experiments where both B and C cultures were negative that the whole cavity or even that the tract of dentine penetrated by the burr was free from living organisms because some bacteria may not have found the standard media suitable for their growth. However, a comparison of the results of a series of experiments with one germicidal agent against the results of a series with another agent enables the germicidal efficiency for carious dentine of these agents to be compared. An index of bactericidal efficiency for each agent was obtained by comparing as a percentage the number of experiments with negative cultures (i.e. both B and C cultures being negative) with the total number of experiments performed with that agent.

As this bacteriological section of the present research is assessed statistically, it suffers from all the disadvantages inherent in a statistical approach to any biological problem. When worked out mathematically the variations in indices which can reasonably be accounted for by chance are often found to be unexpectedly large. Therefore small differences in the indices of germicidal agents cannot be regarded of significance, especially if few experiments have been performed to obtain the data for working out the germicidal index.

#### THE RESULTS OF THE BACTERIOLOGICAL INVESTIGATION

The results of the main bacteriological investigations are shown in the table below. Attention should be paid to the number of tests performed to obtain the data from which the bactericidal index was obtained.

#### RESULTS OF A BACTERIOLOGICAL INVESTIGATION ON THE STERILIZATION OF CARIOUS DENTINE BY VARIOUS REAGENTS

| Bactericide<br>(Standard time of application<br>two minutes)                               | Number of experiments<br>performed to obtain data | Approximate concentration<br>(grammes per 100 c.c.) | Bactericidal<br>index |
|--------------------------------------------------------------------------------------------|---------------------------------------------------|-----------------------------------------------------|-----------------------|
| 1. Ammoniacal silver nitrate<br>precipitated with eugenol                                  | 54                                                | —                                                   | 65%                   |
| 2. Saturated aqueous silver<br>nitrate .. .. .                                             | 34                                                | 140                                                 | 74%                   |
| 3. 80% saturated silver fluoride                                                           | 29                                                | 145                                                 | 45%                   |
| 4. Saturated silver chlorate ..                                                            | 23                                                | 10                                                  | 57%                   |
| 5. Saturated cupric nitrate ..                                                             | 38                                                | 100                                                 | 47%                   |
| 6. Saturated copper sulphate                                                               | 16                                                | 35                                                  | 19%                   |
| 7. Saturated zinc iodide ..                                                                | 34                                                | 440                                                 | 53%                   |
| 8. Saturated zinc chloride ..                                                              | 28                                                | 250                                                 | 50%                   |
| 9. 27% aqueous silver nitrate*                                                             | 44                                                | 27                                                  | 39%                   |
| 10. Saturated mercuric nitrate†                                                            | 21                                                | Very soluble                                        | 33%                   |
| 11. Saturated chromic acid ..                                                              | 20                                                | 160                                                 | 50%                   |
| 12. Liquor ammoniæ dilutus ..                                                              | 14                                                | 10                                                  | 29%                   |
| 13. 80% silver fluoride precipi-<br>tated with calcium chlor-<br>ide .. .. .               | 7                                                 | —                                                   | 43%                   |
| 14. 80% silver fluoride precipi-<br>tated with calcium ni-<br>trate .. .. .                | 24                                                | —                                                   | 75%                   |
| Bactericide (standard time of application<br>two minutes)                                  | Number of experiments<br>performed to obtain data |                                                     | Bactericidal<br>index |
| 15. Zinc oxyphosphate cement liquid .. .. .                                                | 20                                                |                                                     | 50%                   |
| 16. Zinc oxyphosphate cement liquid precipitated with<br>heavy magnesium carbonate .. .. . | 7                                                 |                                                     | 43%                   |
| 17. Hydrogen peroxide (10 volumes) .. .. .                                                 | 15                                                |                                                     | 27%                   |
| 18. Penicillin (50,000 units per c.c.) .. .. .                                             | 20                                                |                                                     | 40%                   |
| 19. 10% aqueous iodine .. .. .                                                             | 26                                                |                                                     | 27%                   |
| 20. Liquor iodi mitis .. .. .                                                              | 17                                                |                                                     | 29%                   |
| 21. Undiluted metaphen solution .. .. .                                                    | 21                                                |                                                     | 29%                   |
| 22. Undiluted Dettol solution .. .. .                                                      | 17                                                |                                                     | 12%                   |
| 23. Undiluted T.C.P. solution .. .. .                                                      | 15                                                |                                                     | 33%                   |
| 24. Undiluted Milton solution .. .. .                                                      | 22                                                |                                                     | 32%                   |
| 25. Oil of cloves .. .. .                                                                  | 23                                                |                                                     | 30%                   |
| 26. Zinc oxide and oil of cloves dressing‡                                                 | 15                                                |                                                     | 53%                   |
| 27. Copal ether varnish§ .. .. .                                                           | 27                                                |                                                     | 44%                   |
| 28. Ether .. .. .                                                                          | 15                                                |                                                     | 27%                   |
| 29. 95% alcohol .. .. .                                                                    | 18                                                |                                                     | 22%                   |
| 30. Pure phenol .. .. .                                                                    | 13                                                |                                                     | 15%                   |

\*This solution was bought in the form of a prepared solution. It was therefore not fresh. With the exception of the ammoniacal silver nitrate, all the other solutions were freshly prepared before use.

†Mercuric nitrate solution is not highly ionized.

‡§These experiments were not performed under the same conditions as the other agents as:

‡(1) The dressing was left in situ until the time of the bacteriological investigation. (2) A small quantity of caries was removed for retention purposes. (3) Only late tests were performed.

§(1) The varnish was left in situ until the time of the bacteriological investigation. (2) Only late tests were performed.

### THE EFFECT OF THE DURATION OF APPLICATION OF THE GERMICIDE ON THE BACTERICIDAL INDEX

27% aqueous silver nitrate was applied to the teeth for periods of one minute, four minutes, or twenty-five minutes, in a series of 51 tests. The variations in the indices were so slight that they cannot be regarded of significance.

#### A COMPARISON OF EARLY AND LATE RESULTS

For each germicide, about half the cultures were inoculated within ten to twenty minutes and half within two and a half to three hours of the application of the germicide to the caries. As only 10 to 15 tests were carried out in each group, only those showing a very marked percentage difference could be regarded as being significant.

With the following agents this difference is of possible significance.

|                                    |         | Early tests | Late tests |
|------------------------------------|---------|-------------|------------|
| Ammoniacal silver nitrate          | ..      | 72%         | 50%        |
| Silver fluoride (80% concentrated) | ..      | 12%         | 71%        |
| Silver chlorate                    | .. .. . | 40%         | 67%        |
| Zinc iodide                        | .. .. . | 69%         | 22%        |
| Penicillin                         | .. .. . | 78%         | 9%         |

It will be noted that ammoniacal silver nitrate, zinc iodide and penicillin, all of which are liable to be broken down rapidly in carious tissue, show as would be expected, higher indices in the early tests.

#### A COMPARISON OF THE GERMICIDAL INDICES OF AQUEOUS SOLUTIONS OF THE NITRATES OF SILVER, COPPER AND ZINC

Aqueous solutions were prepared so as to contain equal numbers of silver, copper and zinc ions and of nitrate ions, assuming all the salts were fully ionized. Compared with zinc and cupric nitrate solutions, the deficiency of nitrate ions in silver nitrate solutions was made up by the addition of sodium nitrate. Sodium ions are unlikely to have a highly germicidal action. To allow for any slowness of penetration, the solutions were applied for a standard time of four minutes instead of two.

|                    |           | Tests performed | Bactericidal index |
|--------------------|-----------|-----------------|--------------------|
| Silver nitrate 30% | } .. .. . | 25              | 64%                |
| Sodium nitrate 14% |           |                 |                    |
| Zinc nitrate 33½%  |           | 26              | 50%                |
| Cupric nitrate 33% | .. .. .   | 21              | 43%                |

The silver solution is seen to be more effective than either the cupric or zinc solutions. The variations between the indices for the cupric and zinc salts are not sufficient to be regarded as significant.

#### DISCUSSION

An examination of the bactericidal indices of the 30 solutions investigated shows that, on the whole, the soluble salts of the heavy metals have the greatest bactericidal action.

If we consider only those soluble salts of heavy metals which are highly ionized in aqueous solution we find that, the more concentrated the solution of the salts, the higher are the germicidal indices.

|   |                                  | Approximate concentration (grammes per 100 c.c.) | Germicidal index |
|---|----------------------------------|--------------------------------------------------|------------------|
| { | Saturated aqueous silver nitrate | .. .. . 140                                      | 74%              |
|   | 80% saturated silver fluoride    | .. .. . 145                                      | 45%              |
| { | Saturated silver chlorate        | .. .. . 10                                       | 57%              |
|   | Saturated copper nitrate         | .. .. . 100                                      | 47%              |
| { | Saturated copper sulphate        | .. .. . 35                                       | 19%              |
|   | Saturated zinc iodide            | .. .. . 440                                      | 53%              |
| { | Saturated zinc chloride          | .. .. . 250                                      | 50%              |

Two notable exceptions are observed. Silver fluoride is a less effective and silver chlorate a more effective germicide than would be expected.

In 1918 Eisenberg did some extensive research on the toxic effect of ions on bacteria. In general the toxicity of ions may be stated to be:

#### Cations

Silver > Mercury > Copper > Zinc > Calcium > Ammonium > Potassium > Sodium.

#### Anions

Hydroxide > Fluoride > Chromate > Monobasic Phosphate > Perchlorate > Iodide > Hypophosphite > Chlorate > Sulphite > Nitrate > Chloride > Sulphate.

On the whole, the observed bactericidal indices are explained by this order of toxicity. However, silver fluoride should still have had a more highly germicidal action for both silver and fluoride radicles are highly bactericidal and silver fluoride is very soluble. This may be explained if we consider the composition of dentine. In the process of decalcification such as occurs in caries, there are present in carious dentine a few calcium and phosphate ions. On the application of silver fluoride, the fluoride will be decomposed with the formation of the practically insoluble calcium fluoride and silver phosphate. This will immediately reduce the bactericidal action of the silver fluoride by:

(1) Withdrawing the highly bactericidal fluoride ions.

(2) Forming an insoluble precipitate on the surface which will impede further rapid penetration of other ions.

A similar reaction resulting in the formation of precipitates when the germicide is applied to carious dentine is probably occurring with copper sulphate and aqueous silver nitrate. Some experiments were performed to see if this were possible:

Immediately after extraction, some teeth were immersed in a 5% sodium chloride solution at blood heat for half an hour. Subsequently the carious cavities were dried and either ammoniacal silver nitrate or concentrated aqueous silver nitrate was applied. The bactericidal index was assessed in the usual way.

|                                  | Bactericidal indices | After previous treatment of teeth with 5% sodium chloride |
|----------------------------------|----------------------|-----------------------------------------------------------|
| Saturated aqueous silver nitrate | 74%                  | 33%                                                       |
| Ammoniacal silver nitrate        | 65%                  | 92%                                                       |

This shows that the presence of the chloride ions has markedly reduced the germicidal action of the aqueous silver nitrate. The germicidal efficiency of the ammoniacal solution, however, actually appears to have been enhanced but this may be accounted for by the toxic action of the hypertonic saline solution in which they were previously immersed for thirty minutes.

This phenomenon may be explained as follows: Silver chloride (solubility 0.00015 gramme per 100 c.c.) and silver phosphate (solubility 0.002 gramme per 100 c.c.) are nearly insoluble in water. Both are more soluble in ammonia. If the ammoniacal silver nitrate is applied to carious dentine, any great reduction in the germicidal action due to the presence of chloride or phosphate ions will therefore largely be avoided. When the concentration of the chloride ions was markedly increased in these experiments, the differences between the actions of the aqueous and ammoniacal solutions became apparent.

Consideration of these results has enabled us to suggest certain of the properties which it is desirable that any salt, which is highly ionized in aqueous solution, should have in order to be an effective germicide of carious dentine. It is not suggested that these represent the only properties necessary.

(1) Its basic radicle should be highly bactericidal.

(2) Its acidic radicle should also be highly bactericidal.

(3) The salt should have a high solubility in water.

(4) The acidic radicle should not react with the calcium salts present in carious dentine to form an insoluble salt.

(5) Similarly, the basic radicle should not react with the phosphates present in carious dentine to form an insoluble salt.

(6) If a self-limiting action following its application to freshly opened dentinal tubules is desired, the chloride of the basic radicle should be insoluble in order that it may be precipitated by the tissue fluid chlorides.

(7) If the salt is easily reduced, it will act more quickly as a germicide and at the same time will be precipitated rapidly by the tissue fluid proteins, making it more self-limiting in its action on vital dentine.

Silver nitrate fulfils nearly all these conditions and therefore its clinical use for sterilizing carious dentine is justified.

Unfortunately silver salts tend to stain the tooth substance markedly. Copper and mercury do so also to a lesser degree. Zinc salts, however, do not. Zinc iodide and chloride are moderately successful germicides but it should be noted that:

(1) They are both liable to be more irritating to the pulpal tissue because zinc chloride is not precipitated by the tissue fluid chlorides.

(2) Zinc iodide is a very unstable salt and should be used freshly and kept free from moisture.

With regard to the remaining germicides investigated, the more complex chemical compounds have relatively low bactericidal indices. This is at variance with the findings of Seltzer (1942) who found that the chlorphenolates and metaphen were good germicides for sound dentine.

Hydrogen peroxide is not effective because it is decomposed by the surface debris of the carious cavities. This is readily shown by the vigorous frothing following its application to the caries.

Zinc oxyphosphate cement liquid is shown to have an appreciable germicidal effect which may be of clinical importance, especially if the mix of the cement is thin. This effect can be explained satisfactorily owing to the high hydrogen-ion concentration and the toxicity of the phosphate ions. This toxicity is unlikely to be specific to bacteria and therefore, as one would expect, it will be irritating to the pulp if it should come into contact with it.

The bactericidal index of copal ether varnish is surprisingly high but it should be noted that the varnish was allowed to remain in situ for two and a half to three hours.

The relatively high germicidal index of zinc oxide and oil of cloves may be explained by:

(1) A small quantity of caries having been removed for retention purposes.

(2) It was allowed to remain in situ for two and a half to three hours.

Alcohol, ether, and phenol have little value in sterilizing carious dentine.

#### THE HISTOLOGICAL RESEARCH

The second phase of the present research was entirely histological and was undertaken to elucidate two problems.

(1) To demonstrate the possible effects on the pulp of the more successful germicidal agents applied to carious dentine.

(2) To show the depth of penetration of the germicidal agents into the carious tissue.

Attention has been mainly concentrated on the use of silver nitrate as the germicidal agent, first because it is the most effective germicide which has been investigated, and secondly because the silver can be demonstrated so easily in the tissues.

It is well known that the bactericidal and toxic action of silver preparations varies considerably. Thus Pilcher and Sollmann (1924) state that the inhibiting concentrations for growth of yeasts of aqueous solutions of various silver preparations is as follows:

|                         |                       |
|-------------------------|-----------------------|
| Silver nitrate          | 1 : 40,000            |
| Protargol               | 1 : 5,000 - 1 : 3,000 |
| Colloidal silver iodide | 1 : 10                |

Completely insoluble precipitates will have even less bactericidal and toxic action. Silver as seen in histological preparations will not necessarily be in the same condition as it existed in the tissues before the preparation of the slides, because reduction of the silver may have taken place during the fixation of the tissue by formalin or even by exposure to light. Insoluble and therefore relatively non-toxic precipitates will be easily visible under the microscope but if a 1 : 10,000 silver nitrate solution could be maintained in ionic form it would be lethal to bacteria but not readily visible microscopically. One is, however, justified in assuming that completely isolated granules of silver precipitates will not possess any great toxic or bactericidal action. On the other hand, diffuse staining of the tissues will probably denote that at some time prior to reduction the silver existed in such a form as to be toxic to the tissues and bacteria in that area. Further evidence for these statements will be given later.

#### THE INTERPRETATION OF THE PHOTOMICROGRAPHS

The photomicrographs which illustrate this paper have been selected from fields in over 500 histological slides prepared from teeth treated experimentally with silver nitrate and other germicides. In the original slides the silver precipitates could be distinguished from the basic staining with hæmatoxylin-eosin, Gram's, Van Gieson's or similar stains. In black and white photomicrographs the distinction is not so evident and so an effort has been made to indicate the less obvious silver precipitates.



# THE EFFECT OF THE APPLICATION OF SILVER NITRATE TO EXPOSED VITAL DENTINE

Cavities were prepared in about a dozen sound teeth with a slow-rotating handpiece and ammoniacal or aqueous silver nitrate was applied to the exposed dentine for two minutes. In the case of the ammoniacal solutions, the silver nitrate was reduced with eugenol. The cavities were dressed with zinc oxide and oil of cloves and the teeth extracted at periods from fifteen minutes to fifteen days later. Microscopic examinations of these teeth shows that: (1) The silver is, in the majority of cases, strictly limited to the dentinal tubules opened by the cutting of the cavity (figs. 1 and 2).

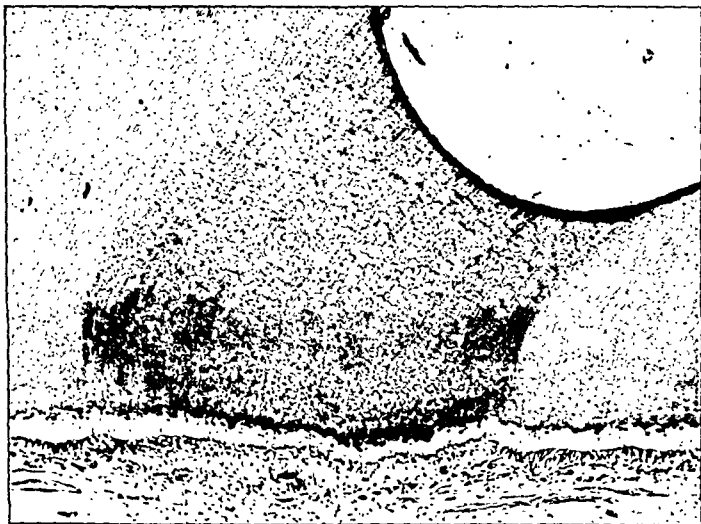


FIG. 1.—Labial cavity. Upper incisor. *Treatment:* Ammoniacal silver nitrate. Dressed zinc oxide and oil of cloves. Extracted fourteen days later. *Preparation of slide:* Decalcified section. Staining hæmatoxylin-eosin.  $\times 50$ .

NOTE.—(1) Strict localization of the silver staining to the cut dentinal tubules. (2) No silver has penetrated into the pulp. (3) The odontoblast layer is only disorganized under the affected tubules.

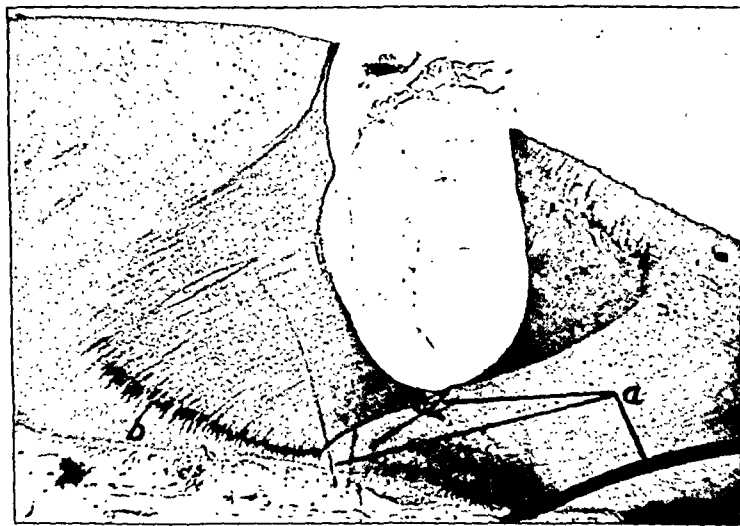


FIG. 2.—Buccal cavity. Upper premolar. *Treatment:* Ammoniacal silver nitrate. Dressed zinc oxide and oil of cloves. Extracted fourteen days later. *Preparation of slide:* Decalcified section. Stained hæmatoxylin-eosin.  $\times 30$ . Key: (a) Creases in section. (b) Zone of tubular blockages.

NOTE.—(1) Extension of area of silver staining towards the amelo-dentinal junction. (2) The denseness of the precipitate at the periphery of the stained area.

(2) If any tubules are opened to the pulpal side of the amelo-dentinal junction, the silver will track not only pulpally but also in the majority of cases to a nearly equal extent towards the amelo-dentinal junction (fig. 2).

(3) In those cases in which the silver has been satisfactorily applied, the silver is seen to have penetrated very close to the pulpal surface (figs. 1 and 2), but only in rare cases is there any evidence of the silver having been carried actually into the pulp (fig. 3).

(4) The silver is seen to exist: (a) As large, discrete granules (fig. 4). (b) As very fine diffuse staining (fig. 4) which, as close examination under an oil immersion lens shows, occurs mainly on the walls of the dentinal tubules and their lateral communication.

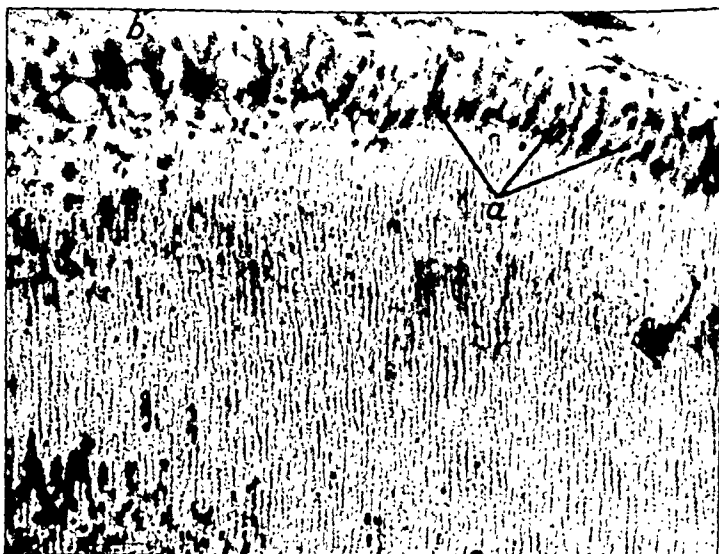


FIG. 3.—Labial cavity. Upper canine. Treatment: Ammoniacal silver nitrate. Dressed zinc oxide and oil of cloves. Extracted eight days later. Preparation of slide: Decalcified section. Staining hæmatoxylin-eosin.  $\times 260$ . Key: (a) Silver granules in a relatively normal odontoblast layer, cut slightly obliquely, lying under tubules containing only isolated granules of silver. (b) Disorganized odontoblast layer below zone of tubule blockages. No silver granules are visible in this area.

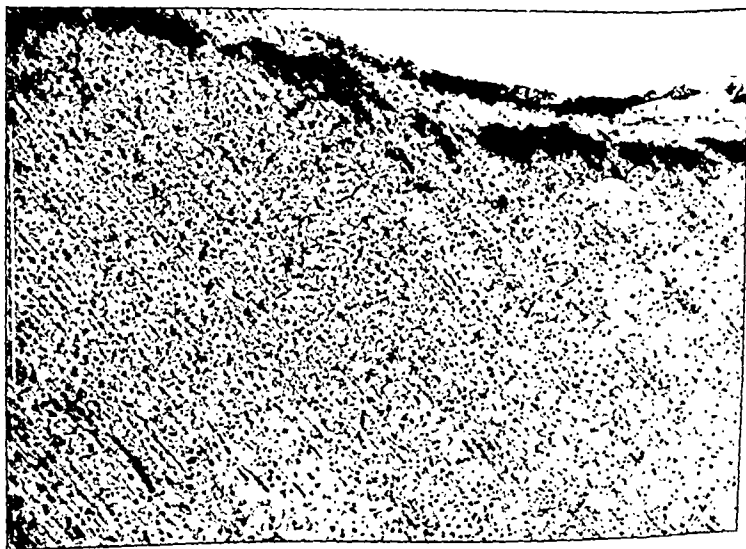


FIG. 4.—Same tooth as in fig. 3.  $\times 260$ .

NOTE.—Large discrete silver granules and very fine diffuse silver staining of tissues.

(c) As dense dentinal tubule blockages which appear to outline the dentinal fibril for about  $5\text{--}10\mu$ . These occur usually towards the pulpal surface near the periphery of the area of penetration (fig. 5) but what are probably analogous precipitates are seen in the most laterally opened dentinal tubules (fig. 6).

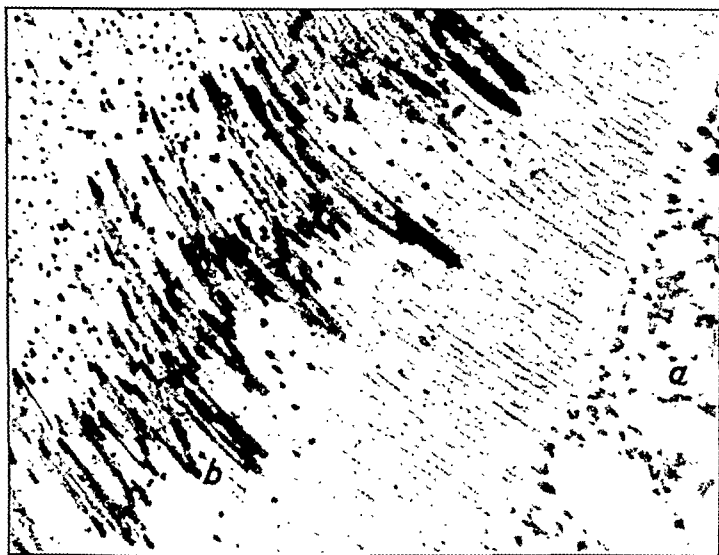


FIG. 5.—Same tooth as in fig. 2.  $\times 440$ . Key: (a) Disorganized pulpal tissues. (b) Tubular blockages.

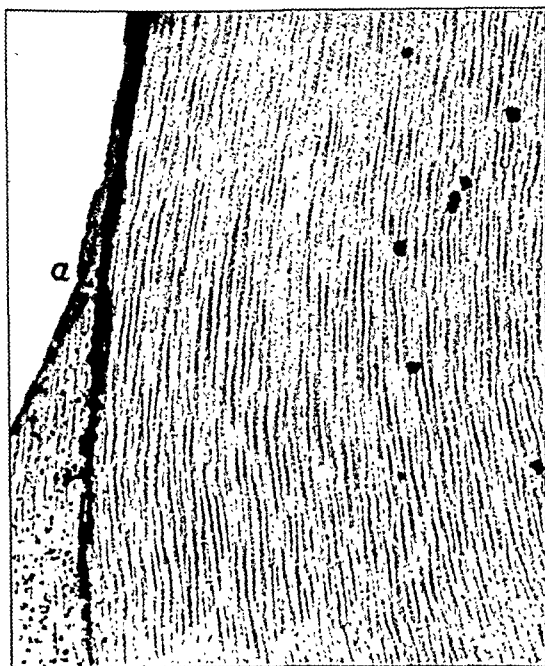


FIG. 6.—Same tooth as in fig. 3.  $\times 240$ . Key: (a) Cavity surface.

(5) Wherever there is evidence of a thorough impregnation with silver nitrate, the silver is seen to penetrate the finest tissue fluid channels, including the lateral branches of the dentinal tubules (fig. 7). Close examination of these slides under an oil immersion lens, with fine focusing up and down, shows an appearance extremely suggestive of lateral branches of dentinal fibrils lying within lateral branches of the dentinal tubules (fig. 8). The fibrils have probably become shrunken owing to their treatment. Large molecules of methylene-blue and particles of indian ink do not readily penetrate into the lateral branches of the dentinal tubules. It is possible that the complex chemical germicides also do not penetrate into fine spaces to any marked extent and that this may account for their comparative lack of success in sterilizing carious dentine.



FIG. 7.—Labial cavity. Upper incisor. *Treatment*: Ammoniacal silver nitrate precipitated with eugenol. Extracted twenty-five minutes later. *Preparation of slide*: Decalcified section. Staining hæmatoxylin-eosin.  $\times 445$ . Key: (a) Amelo-dental junction, (b) Cavity surface, (c) Dentinal tubule.



FIG. 8.—Same tooth as in fig. 3.  $\times 500$ . Key: (a) Terminal branch of a dentinal fibril lying within the terminal branch of a dentinal tubule. (b) ? lateral branch of a dentinal fibril lying within a lateral branch of a dentinal tubule. (c) Cavity surface, (d) Amelo-dental junction.

## SOME COMMENTS ON THE STAINING OF VITAL DENTINE AND THE PULPAL REACTIONS FOLLOWING THE APPLICATION OF SILVER NITRATE

Silver nitrate solutions applied to vital dentine will quickly diffuse into that space, containing tissue fluid, lying between the dentinal fibril and the tubule wall. This tissue fluid will have a composition approximately similar to that of tissue fluid elsewhere in the body and will contain chlorides, phosphates and proteins. The silver will quickly react with all these three forming insoluble precipitates. If there is sufficient silver, these particles of silver compounds will grow in size as they are carried along the dentinal tubules, rather like a snowball rolled over snow-covered ground. Ultimately they will become so large that they will impact within the tubules. At the same time, owing to the precipitation of the chlorides, phosphates and proteins in the more peripheral parts of the dentinal tubules, diffusion and osmotic currents will cause further chlorides, phosphates and proteins to flood out peripherally from the tissue fluid spaces of the pulp. These will react with any unprecipitated silver diffusing pulpally, producing still further precipitates in the vicinity of the tubular "blockage". Similar blockages will occur in other areas near the periphery of the area of silver penetration. Thus the silver eventually becomes effectively isolated in that leash of dentinal tubules which have been opened by the cutting of the cavity. Before the blockage becomes complete, silver in a highly toxic form may have diffused into the pulp, thus producing a severe reaction (fig. 9).

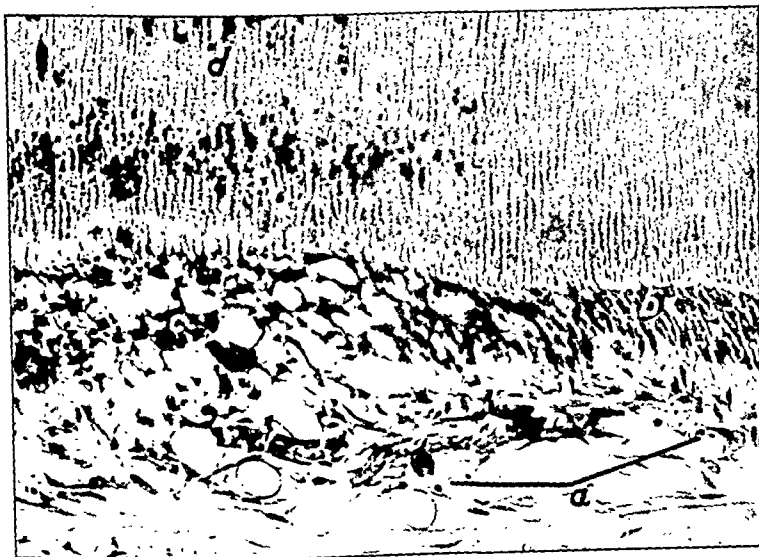


Fig. 9.—Same tooth as in fig. 3.  $\times 260$ . Key: (a) A few isolated silver granules in pulpal tissues. (b) Normal odontoblast layer, cut slightly obliquely. (c) Disorganized odontoblast layer below zone of tubular blockages. (d) The end of a tubular blockage.

In those cases in which relatively small concentrations of silver track into the dentinal tubules, the whole of the silver will be precipitated nearly instantaneously by the tissue fluid chlorides, phosphates and proteins. Coarse granules of silver will be formed but as there is no excess of silver in the tubules, will not grow beyond a certain stage. Impaction of the granules will not occur and therefore they will be free to be carried by diffusion currents and possibly by tissue fluid flow down to and at times actually into the pulp. This precipitated silver cannot be expected to have any marked toxic action on protoplasm whether in the form of the cells of the pulp or of bacteria. We find that such isolated granules of silver produce little inflammatory reaction in the pulpal tissue (fig. 3).

Sections of teeth fixed in formalin within fifteen minutes of the application of the silver nitrate to the vital dentine show the silver nitrate may already have penetrated nearly to the pulpal surface of the dentine (fig. 10).

Consideration of the histological appearances of teeth treated by the application of silver nitrate to exposed vital dentine has shown that:

(1) Silver nitrate solutions are able to penetrate rapidly through non-carious dentine to considerable depths but seldom enter the pulp.

(2) The silver precipitates seen in these sections may represent silver that was originally highly toxic and bactericidal or silver that was relatively non-toxic. The more toxic forms are indicated by a diffuse staining of the tissues; the relatively non-toxic forms by large, discrete granules.

(3) In cases of thorough impregnation by silver, the silver is able to penetrate into very narrow tissue fluid channels such as the lateral communications of the dentinal tubules.



FIG. 10.—Same tooth as in fig. 7. (Extracted twenty-five minutes after application of ammoniacal silver nitrate.)  $\times 55$ . The degenerative changes shown in the pulp are not due to the treatment with ammoniacal silver nitrate.

NOTE.—The silver nitrate has penetrated nearly to the pulpal surface of the dentine.

#### A COMPARISON OF THE PULPAL REACTIONS FOLLOWING THE APPLICATION OF VARIOUS GERMICIDES TO THE VITAL DENTINE

In teeth treated by the application of silver nitrate to exposed vital dentine, the pulpal reactions vary from complete disorganization of the odontoblast layer, round-cell infiltration and pulpal hæmorrhages to reactions so slight as to be classed as normal. With both aqueous and ammoniacal solutions, the silver may penetrate nearly down to the pulp. However, in no teeth treated with aqueous solutions has any evidence of thorough impregnation been seen as shown by fine diffuse staining of the dentine; the pulpal reactions of such teeth are correspondingly slight.

In comparison with the pulpal reactions under cavities treated with other germicidal agents, including the zinc chloride, the reactions with both the ammoniacal and aqueous silver nitrate are usually slight. It is, however, unwise to be too dogmatic because in the case of these other germicides there is no way of assessing their degree of penetration as no visible precipitates are produced.

#### THE EFFECT OF THE APPLICATION OF SILVER NITRATE TO CARIOUS CAVITIES

Microscopical examination of carious cavities which have been treated with silver nitrate enables the following zones of silver staining to be distinguished (fig. 11).

(1) A dense black superficial zone of staining in which all structural detail is lost owing to the denseness of the stain. This zone varies in thickness up to 1 mm. in depth.

(2) An intermediate zone of brown staining where all structural detail has not been lost. It is difficult to be certain how much of this brown staining is due to the carious process and how much is due to the silver.

(3) A deep zone containing coarse granules of silver. This extends in some cases to the depth of 2 mm. from the surface of the cavity. In some cases they may represent silver-stained bacteria. On the whole the granules become larger the deeper they are in the tissues. (This corresponds to the picture found in non-carious dentine.) Beyond that level relatively fine granules are often seen in the dentinal tubules and are thought to represent silver-stained bacteria.

THE HISTOLOGICAL EVIDENCE REGARDING THE DEPTH OF PENETRATION OF SILVER NITRATE  
FOLLOWING ITS APPLICATION TO CARIOUS TISSUES

Owing to the ease with which silver precipitates may be demonstrated in histological preparations, there is no difficulty in assessing the depth of penetration of silver nitrate or its breakdown products. The depth of the carious tissue may also be assessed with reasonable accuracy by the usual appearances such as liquefaction foci, typically stained bacteria, &c. In sections stained with such stains as Gram's, the presence of typically stained bacteria is positive evidence that the tissue was infected. It is also highly probable that such bacteria had not been killed by the application of the silver nitrate as they would have become silver-stained, thus masking the less intense strain. One is therefore justified in assuming that such cavities had not been sterilized by the silver nitrate.

In several of the carious teeth treated with silver nitrate before decalcification an in-

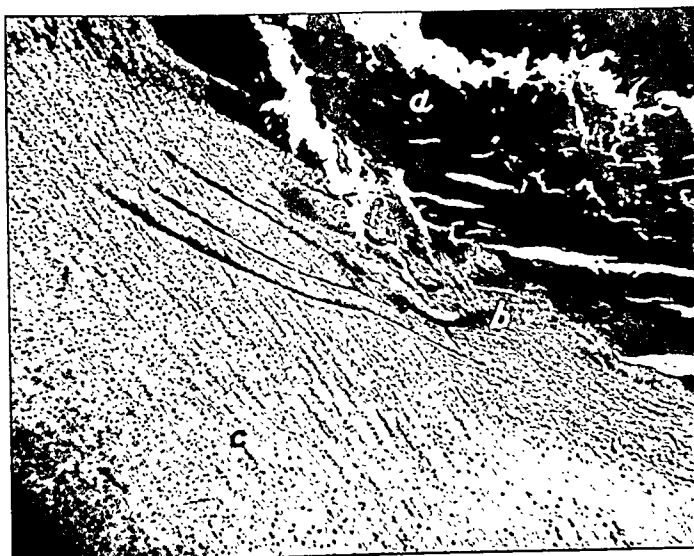


FIG. 11.—Deep occlusal cavity in upper premolar. *Treatment:* Ammoniacal silver nitrate and eugenol thirty minutes before extraction. *Preparation of slide:* Decalcified section. Staining hematoxylin-eosin.  $\times 50$ . *Key:* (a) Dense black superficial zone of staining. (b) Intermediate zone of brown staining. (c) Deep zone containing coarse granules of silver.

teresting appearance has been observed which is thought to represent an early sign of acidogenic and proteolytic attack (fig. 12). It may arise purely from physical causes or be due to a Liesegang phenomenon. Alternatively it may be caused as follows: As the dentine is attacked by the acids and the organic matrix digested by the proteolytic enzymes, the process does not occur to an equal extent along the length of the tubules but is greater at regular intervals of about 4 microns. Such decalcified and partially digested tissue will take the silver staining. The first signs of carious attack are therefore shown as annular striations around the walls of the tubules and even of their lateral communications. This appearance is well seen in oblique sections. As more of the matrix is attacked, the striations around the walls of the neighbouring tubules coalesce producing linear markings through the intervening matrix.

Judging the depth of the caries by these microscopical appearances it may be stated that the histological evidence shows that silver nitrate applied to the carious surface will not penetrate through the complete depth of all cavities. It often penetrates to depths of 2 mm., and in all sections examined penetrated at least 1 mm. in depth. It cannot, however, be assumed that all tissue to which the silver has penetrated has been sterilized because much of the silver in the deeper zones exists in the form of discrete granules which, it has been shown, has little bactericidal or toxic action. On the other hand, it can also be stated that barriers preventing the penetration of the silver through the carious tissue seldom exist and there would appear to be no reason why silver nitrate should not sterilize the more shallow cavities completely.

## A NOTE ON OTHER PRACTICAL APPLICATIONS OF THE PRESENT RESEARCH

Many of the principles which effect the depth of penetration and the toxicity to the pulpal tissues of germicidal agents should be equally applicable to any dressing applied to exposed vital dentine. This is especially true in the case of cavity linings such as dental cements. Thus it seems probable that the irritant properties of many cement linings will be found to be due not only to their hydrogen-ion concentration but also to a lesser degree to other radicles in the composition of the cement. It might also be possible to manufacture

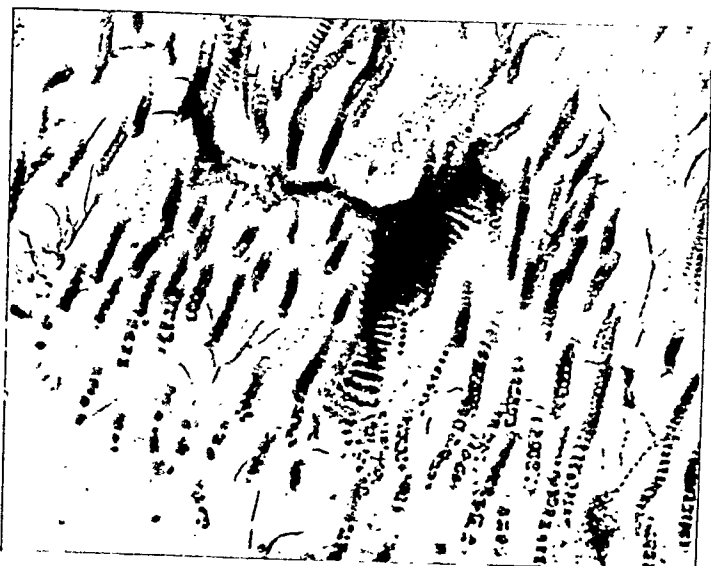


FIG. 12.—Occlusal cavity upper molar. *Treatment:* Ammoniacal silver nitrate and eugenol ninety minutes before extraction. *Preparation of slide:* Decalcified section. Haematoxylin-eosin staining.  $\times 610$ . The section has been cut slightly obliquely and lies in an area of secondary dentine.

cements which would be less irritant to the pulp owing to being naturally self-limiting in their action in a similar way to silver nitrate which is readily precipitated in a relatively non-toxic form by the tissue fluids.

## SUMMARY

A bacteriological investigation into the efficiency of over thirty agents as bactericides for carious dentine has been carried out. It has been shown that the soluble salts of the heavy metals, as a group, are most successful in the sterilization of carious dentine. Of these, silver nitrate, either in the ammoniacal or the concentrated aqueous form, is the most effective. The soluble zinc salts such as zinc iodide and zinc chloride are not as efficient for sterilizing dentine but will not stain the tooth substance.

Examination of histological sections of teeth in which cavities were prepared and which were treated with various bactericides shows that silver nitrate applied to exposed vital dentine produces a remarkably slight reaction in the pulpal tissues. This is due to the precipitation of the silver nitrate in a less toxic form by the tissue fluid chlorides, phosphates and proteins within the dentinal tubules. The precipitation results in diffusion currents from the tissue fluid spaces of the pulp. In the majority of cases the silver nitrate is, therefore, unable to exert its toxic effect on the cells of the pulp as it is precipitated in insoluble and less toxic forms before it is able to reach them. These insoluble precipitates may be carried down the tissue fluid spaces of the pulp and peripherally into other dentinal tubules without causing gross damage to the cells with which they come into contact.

In cases of successful applications of the ammoniacal silver nitrate to exposed vital dentine, it is seen to penetrate the tissue fluid channels of the dentine, including the lateral communications of the dentinal tubules. Applied to carious dentine, the superficial layers of the caries become thoroughly impregnated with the silver salts; the deeper layers may also be seen to contain silver particles which, however, are thought to represent silver in a less toxic and bactericidal form.



*Acknowledgments.*—My thanks are especially due to Professor H. F. Humphreys and Professor J. D. Shrewsbury for providing the facilities for this research and to Mr. E. B. Manley, Dr. J. Abiss, Mr. F. W. Moore and Mr. E. B. Brain for the help and advice they have so willingly given.

#### REFERENCES

- EISENBERG, P. (1918) *Zbl. Bakt., Abt. 1, Orig.*, 82, 69.  
 PILCHER, J. D., and SOLLMANN, T. (1924) *J. Lab. clin. Med.*, 9, 256.  
 SELTZER, S. (1942) *J. dent. Res.*, 21, 269.

## Penicillin in the Treatment of Dead Teeth

By W. G. CROSS, M.B., M.S., B.D.S.

*Department of Periodontia, Institute of Dental Surgery, London, W.C.1*

In recent years there have been a number of references in the literature to the use of penicillin in the treatment of infected root canals, principally in the United States of America. The methods of treatment have varied. Cipes (1946) injected penicillin in sesame oil into the root canal in the concentration of 5,000 units per c.c. Buchbinder in 1946 treated 36 cases also by injecting up the root canal. Later (1947) he pointed out that there were three main methods of treatment. The first was to inject penicillin with procaine into the peri-apical region. The second was to irrigate the canal with penicillin solution, and the third was the introduction of penicillin-impregnated points into the canal. In the last-mentioned method the points contained 3,000 units of penicillin and were removed after intervals varying from one to seven days. Those remaining in the canal for forty-eight hours, or longer, were still found to exhibit bacteriostasis. Bender (1947), using penicillin in a solution containing 25,000 to 50,000 units per c.c., irrigated the canals in 53 cases, using at least 1 c.c. Of these, 37 were rendered sterile in one treatment; 16 did not respond. As the volume of the root canal is only about 0.2 c.c. on the average, the effective dosage cannot have been more than 5,000 to 10,000 units per application.

In his most recent method, Buchbinder (1948) uses points containing 3,000 units of penicillin, either dry or moist, having flushed out the root canal with penicillin in solution. Out of 44 cases, 23 were rendered sterile in one treatment, 6 in two treatments, 3 in three treatments, 2 in four treatments, 2 in five treatments and 5 in six treatments. 3 were not sterilized and were found to contain penicillin-resistant organisms. Treatment of the average case occupied two visits. The dry points were prepared by placing paper points soaked in penicillin solution in a vacuum desiccator.

Less successful results were obtained by Rasmussen (1948). His technique was to insert paper points containing either 2,500 or 5,000 units of penicillin—whether wet or dry is not mentioned—after forcing under pressure about 1 c.c. of a solution containing from 20,000 to 100,000 units of penicillin up the root canal. He found that of the 29 cases examined, no less than 18 had penicillin-resistant organisms; of the 11 penicillin-sensitive cases 5 only were sterilized.

In this communication the results of treatment of a small number of cases treated at Guy's Hospital Dental School are shown. 18 teeth were treated. The results are represented in Tables I to IV.

*Selection of cases.*—For choice, a dead tooth was selected in which no attempt to open up the root canal had been made. Such teeth were those which had died as a result of trauma or a silicate filling. In addition, a few teeth where the pulp chamber had already been opened were treated.

*Technique.*—The tooth is isolated with rubber dam, painted with tincture of iodine, the pulp chamber entered with a sterile burr and a bacteriological culture made. This is done by the introduction of a sterile paper point which is immediately placed in nutrient broth and sent to the laboratory.

At the same visit the root canal contents are removed aseptically and a penicillin-impregnated paper point<sup>1</sup> inserted and sealed with oxyphosphate cement.

By the next visit, two days later, there will be laboratory information as to whether there are micro-organisms present and, if so, whether they are penicillin-sensitive. The paper point which was inserted at the first visit is removed, placed in broth and sent for culture. At the same time an additional sterile point is inserted, removed, and also sent to the laboratory.

<sup>1</sup>100 paper points are placed in a penicillin ampoule containing 1 mega unit of crystalline penicillin in 1.5 c.c. of sterile distilled water. This ampoule is placed in a vacuum desiccator ( $\text{CaCl}_2$ ) for forty-eight hours, and at the end of this time the points are dry but stuck together. They are then teased apart by two pairs of sterile forceps and stored in a screw-capped sterile glass bottle.

If the first report indicates the presence of penicillin-sensitive organisms, a second penicillin point is inserted and sealed as before. The oxyphosphate cement is used as a stiff mix; only sufficient to fill up the entrance to the pulp chamber is inserted and care is taken that the point does not project through the cement.

At the third visit, four days from commencement, the penicillin point is removed. If the previous one yielded no growth on culture, a further penicillin point is sealed in and the one just removed is sent for culture.

If at the fourth visit, six days from commencement, both the preceding points still yield no growth on culture, the root canal is filled.

The tooth is then X-rayed and periodically re-examined. At present, no case has been treated for more than fourteen months.

### PENICILLIN-TREATED DEAD TEETH — 18 CASES

TABLE I.—BACTERIOLOGICAL RESULTS. (INITIAL CULTURE)

| Result of culture            | No. of teeth | Micro-organisms                | No. of teeth |
|------------------------------|--------------|--------------------------------|--------------|
| Positive .. .. .             | 12           | <i>Strep. viridans</i> .. .. . | 7            |
| Negative .. .. .             | 5            | <i>N. catarrhalis</i> .. .. .  | 3            |
| Report not available .. .. . | 1            | <i>B. friedländeri</i> .. .. . | 1            |
|                              |              | <i>Staph. aureus</i> .. .. .   | 1            |

TABLE II.—BACTERIOLOGICAL RESULTS. (CULTURE AFTER FORTY-EIGHT HOURS PENICILLIN THERAPY)

| Result of culture               | No. of teeth | Micro-organisms                | No. of teeth |
|---------------------------------|--------------|--------------------------------|--------------|
| Positive .. .. .                | 2            | <i>N. catarrhalis</i> .. .. .  | 1            |
| Negative .. .. .                | 14           | <i>B. friedländeri</i> .. .. . | 1            |
| Patients did not return .. .. . | 2            | <i>Strep. viridans</i> .. .. . | 1            |
|                                 |              | <i>M. flavus</i> .. .. .       | 1            |

TABLE III.—CLINICAL RESULTS

|                                             | No. of teeth |
|---------------------------------------------|--------------|
| No signs or symptoms .. .. .                | 12           |
| Pain, &c., necessitating apicectomy .. .. . | 3            |
| Patients did not return .. .. .             | 3            |

TABLE IV.—RADIOGRAPHICAL RESULTS\*

|                                                 | No. of teeth |
|-------------------------------------------------|--------------|
| Smaller, more circumscribed apical area .. .. . | 11           |
| Unchanged (normal initially) .. .. .            | 1            |
| Patients not available .. .. .                  | 6            |

\*Average time after initial treatment—ten to twelve months.

### RESULTS

From these results it will be seen that in certain cases penicillin-impregnated points can rapidly sterilise the root canal. It is probable that penicillin-sensitive organisms in the lateral and apical canals will be reached by the antibiotic owing to its ready diffusibility, even in the presence of blood, pus and necrotic tissue.

In the cases of failure it was found that penicillin-insensitive organisms were present to the extent of a very few colonies. When the penicillin had produced the disappearance of the sensitive organisms, the insensitive ones were enabled to multiply.

Such cases should be treated either by chemical methods and apicectomy, or perhaps by the combination of penicillin with a drug capable of destroying the Gram-negative organisms, e.g. streptomycin, as suggested by Bartels and Buchbinder (1949).

### CONCLUSION

In cases where cultures from the root canal yield penicillin-sensitive organisms, penicillin-impregnated paper points can be employed to sterilize the canal. In a series of 18 cases 66% were successful clinically and radiographically.

### REFERENCES

- BARTELS, H. A., and BUCHBINDER, M. (1949) *Oral Surg., Oral Med., Oral Path.*, 2, 82.  
 BUCHBINDER, M. (1946) *J. Dent. Res.*, 25, 13.  
 —, and BARTELS, H. (1947) *Amer. J. Orthod. Oral Surg.*, 33, 466.  
 —, and SCHWARTZ, B. S. (1948) *J. dent. Res.*, 27, 211.  
 CIPES, L. R. (1946) *Dent. Items Interest*, 68, 251.  
 RASMUSSEN, B. G. (1948) *Tandlaegebladet*, 52, 243.  
 BENDER, I. B. (1947) *J. Amer. dent. Ass.*, 34, 99.

## Section of Orthopædics

President—H. J. SEDDON, M.A., D.M., F.R.C.S.

[May 3, 1949]

### SYMPOSIUM ON RECONSTRUCTIVE SURGERY OF THE PARALYSED UPPER LIMB

**Professor Robert Merle d'Aubigné:** Treatment of Residual Paralysis After Injuries of the Main Nerves (Superior Extremity).

Although we in France have had some experience in this field, and at my centre at the Hôpital Foch, we have performed about a hundred operations on 82 patients, this subject is, today, a peculiarly British one, and my knowledge of it has been largely acquired here from my friends Seddon, Zachary and Watson-Jones, and from the writings of Robert Jones, Stiles and Forrester-Brown, Sterling Bunnell, Zachary and Hendry.

Of our 82 patients treated for residual paralysis more than half (51) were cases of radial palsy: of the remainder 9 were injuries of the brachial plexus, 5 of the ulnar nerve, 8 of the median, 8 of the ulnar and median and 1 of the musculocutaneous nerve. This, perhaps unexpected, proportion is due to the very good results obtained by tendon transplantation in radial palsy. These results have led us to perform this operation rather early in all cases where recovery by nerve suture seemed unlikely, namely in all defects of the musculospiral nerve in the arm where a graft would have been necessary, and in the high lesions with much scarring. On the contrary, we have attempted suture or grafting in all ulnar and median lesions, where sensibility is of paramount importance, and have been prepared to wait a long time for possible recovery. And our experience of nerve injuries dates only from 1945.

In choosing between the two principal methods of restoring the function of a paralysed arm, namely arthrodesis and muscle transplantation, some general rules must always be borne in mind.

(1) A transplanted muscle invariably loses a great part of its power. This loss may be total or nearly so if, in its new position, the muscle has to work over an angle of soft or, still more, bony parts, or if adhesions develop owing to the muscle or tendon traversing scar tissue. For this reason:

(a) A transplantation has no chance of working if the joints to be moved are stiff.

(b) A muscle to be transplanted must be completely sound. Particularly in brachial plexus paralysis, muscles formerly paralysed cannot be used with a reasonable chance of success unless they have made a perfect recovery.

(c) A transferred muscle is, as a rule, unable to lift the weight of the whole upper extremity.

(d) At the elbow, transplantations may restore movements of the forearm but are unlikely to furnish the strength necessary to push against a considerable resistance or to lift an appreciable weight.

(e) In the hand the transplantation of flexors into extensors gives much better results than the reverse procedure, for extension of hand and fingers never requires strength whereas flexion of fingers needs either strength or precision, or both, if the patient is to use the movement for something other than to provide elegant photographs to put in medical publications. In our experience precision and strength are very inconstant after tendon transfers into paralysed flexors.

(2) Arthrodesis is an irreversible procedure, and, before it is performed, the patient must be warned that, while some movements will be improved, some will be eliminated. At the elbow, where no other joint can supply the movement, we think it is practically never advisable. On the other hand, we have been very happy with the results of arthrodesis of shoulder, and wrist; and we agree with Hendry about arthrodesis of the fingers when one has to be satisfied anyway with a limited function of the hand.

But in no subject are general rules more difficult to establish than in the treatment of residual paralysis of the upper extremity. Every new case is a new problem in itself which must be carefully examined in the light of the state of muscles and nerves and also of the patient's occupation. We will now consider some of the problems which arise in the different regions.

*Shoulder.*—Of the transplantation of the trapezius into the humerus, advised by Lange and Leo Mayer, we have no experience. The conclusions of the American commission in 1942, after study of the end-results in 148 cases, were rather pessimistic. We have, therefore, never attempted this rather complex operation believing, as we have already said, that the chances that a transplanted muscle even as strong as the trapezius could lift the weight of the whole upper extremity over the angle of the acromion were rather problematic.

When the paralysis affects the deltoid with or without the scapulo-humeral muscles and when the muscles moving the scapula are intact, the results of arthrodesis are good. The arm must be abducted at an angle of 40 degrees, with 20 degrees of flexion and 30 degrees of internal rotation. To avoid unduly long immobilization in a big thoraco-brachial plaster, we use a Smith-Petersen or Küntscher nail to fix the head of the humerus to the scapula after freshening the surfaces and introducing cancellous bone grafts. But we agree with Hendry that when many operations are necessary, this should be the last major procedure to be performed.

Birth paralysis of the external rotators of the arm, which we call "obstetrical paralysis", is not a simple paralysis: it is very often associated with deformity of the shoulder and is a muscular "asynergy" rather than an ordinary paralysis. Yet the essential trouble is the impossibility of rotating the arm externally. Since 1945 I have used transplantation of the tendons of *teres major* and *latissimus dorsi* from the volar to the dorsal aspect of the humerus. This tendon transfer, associated with a section of the subscapularis tendon and of the articular capsule when necessary, invariably restores active external rotation of the arm. When the paralysis is localized to the external rotators and the articular deformity

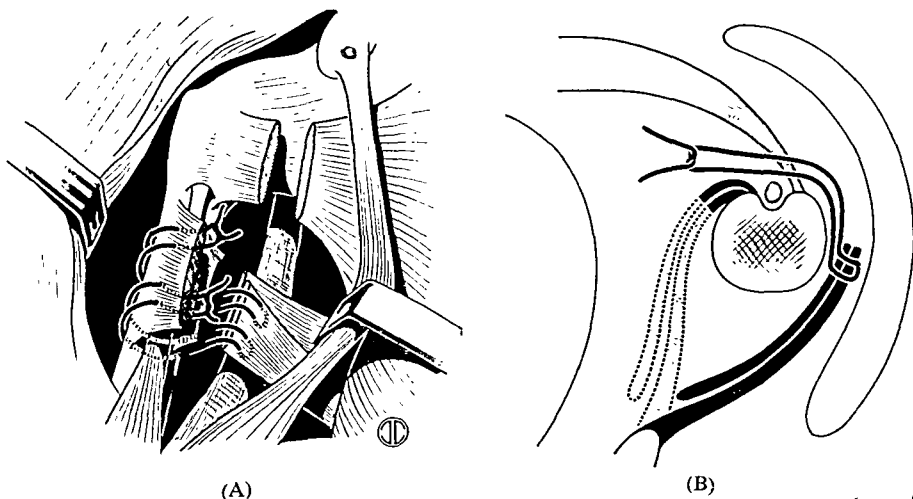


FIG. 1 (A) and (B).—DIAGRAM showing how the silk ligatures threaded through the tendons of *latissimus dorsi* and *teres major* are passed around the humerus and fixed to the *pectoralis major* tendon.

is mild or absent, the patient gains normal active motion of the shoulder after this operation.

L'Episcopo has devised a similar procedure: but he performs it through two incisions, frontal and dorsal, the latter permitting reinsertion of the tendons on the dorsal aspect of the humerus. This second incision can be avoided in the following way: Two stout silk sutures transfix both tendons; the tendons are then cut and the sutures carried around the humerus, first posteriorly then externally (fig. 1). The sutures are threaded through the tendon

of pectoralis major and tied with the arm in full external rotation. This procedure, though perhaps a little more intricate than l'Episcopo's, is simpler and quicker: in girls it can be performed through an axillary incision, leaving no visible scar, a matter of importance in an operation the object of which is almost as much cosmetic as functional (fig. 2).

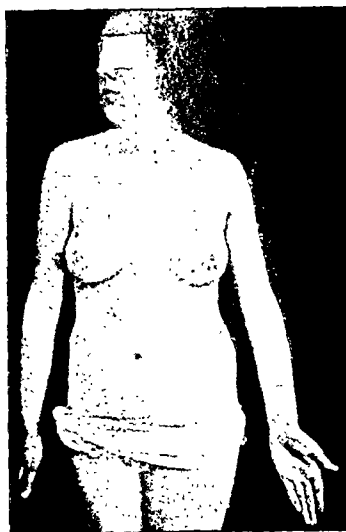


FIG. 2.—Active external rotation of the arm after transplantation of teres major and latissimus dorsi for obstetrical palsy.

*Elbow.*—To restore active extension of the elbow, transplantation of the posterior part of the deltoid into the triceps is a very good method.

To restore flexion, Steindler's operation provides but little strength and has often proved ineffective when brachioradialis as well as biceps is paralysed. During the last two years, transplantation of the lower portion of pectoralis major, as devised by Clark, an operation which we learned from Professor Seddon, has been used in three cases: one is recent; the two others have recovered excellent active flexion, independent of adduction (fig. 3).



FIG. 3.—Active flexion of the elbow six months after a pectoral transplant for complete paralysis of flexors (brachial plexus injury).

*Wrist and hand.*—The function of wrist and hand are so intimately connected that the problems concerning restoration of their movements must be studied at the same time.

Flexion of wrist or fixation by the wrist flexors gives more strength to the extensors of the fingers. Extension of the wrist or fixation by the wrist extensors gives more strength to the flexors of the fingers.

Moreover when the finger flexor or extensor tendons are fixed to the bones of the forearm above the wrist by a scar due to trauma or by tenodesis, extensors of the wrist may be able to flex the fingers, flexors of the wrists to extend the fingers.

These facts must always be borne in mind when planning tendon transfers at the wrist and before deciding on arthrodesis.

There is also a great difference between extension and flexion of the fingers. Extension may be reduced to an elastic action enabling the flexors to move each finger individually. Therefore, this action may be supplied easily by transplanting sound muscles in the extensor tendons: the only important condition is to suture the transplanted tendons with exactly the right tension: if they are too tight flexion will be limited, if too lax extension will be insufficient.

*Radial paralysis.*—For the reasons we have already mentioned, tendon transfer, if correctly executed, can restore a practically normal hand after an irreparable injury of the radial nerve.

Of our 51 cases, the last 40, after our visit to Oxford in 1945, have been operated on by the procedure advised by Zachary. We made but a slight modification: flexor carpi ulnaris is transferred into *all* extensors including extensor indicis proprius and extensor pollicis longus. Palmaris longus is transferred into extensor pollicis brevis and abductor pollicis longus; if palmaris longus is absent, flexor sublimis to the ring finger is used. Separate transplantations into abductor pollicis longus and extensor pollicis longus permit as good extension of the thumb in the plane of the hand as in the plane perpendicular to it.

The results are always good when the tendons are given the right tension.

Arthrodesis of the wrist is never necessary when the radial nerve alone is paralysed.

*Paralysis of flexors and intrinsic muscles of the hand.*—In irreparable paralysis of the median nerve, the ulnar or both, the situation is much more serious and, in most cases, function can only be partially restored.

Three types of procedure are possible:

(a) Arthrodesis of the wrist or fingers allows improved action of the intact or transplanted muscles at the joints left free. Arthrodesis of the wrist permits six muscles (three flexors and three extensors) to be used for transplantation. Since the wrist is ankylosed in slight dorsiflexion, it improves the function of partially recovered flexors of the fingers by making them more tense.

Arthrodesis of the fingers either at the metacarpophalangeal or proximal interphalangeal joint may restore efficiency to flexors of fingers formerly inactive and is a possible weapon against the claw-hand in that a substitute for the paralysed lumbricales is supplied.

(b) Tendon transfers of flexors between themselves is fairly satisfactory but possible only when flexor sublimis is intact. If it is not, transplantation of brachioradialis or the wrist extensors into the finger flexors can be attempted, but the result is less certain.

In our experience Sterling Bunnell's transfer of flexor sublimis into the interosseous tendons is effective only in favourable cases: there must be complete integrity of flexor sublimis, complete freedom of the joints, and very accurate technique.

(c) Another way of transferring the strength of wrist-extensors to finger flexors is tenodesis of the flexor tendons above the wrist. In this procedure, conservation of a free wrist-joint is, of course, essential.

In these paralysed hands the choice of the right procedure is a really difficult problem: there are often two or three possibilities and one cannot always say which will give the patient the most complete recovery.

I will describe the scheme which now guides us in these decisions, though our experience is too limited to permit us to lay down rules.

The first distinction must be made between high lesions of the median or ulnar where the long flexors are paralysed, or, if recovered, are not strong enough for transplantation—and the lesions in the forearm where the long flexors are intact.

*Low lesions.*—*Ulnar nerve:* A patient with an irreparable lesion of the ulnar nerve at the wrist frequently needs no surgical treatment at all. If a manual worker is troubled by

anæsthesia of the little finger and retraction of the ring finger, he will be much improved by amputation of the fifth and transplantation into or arthrodesis of the ring finger.

*Low median nerve lesions* are more serious: very often the delicate function of opposition of the thumb is lost; our best results so far have been obtained by the modified Royle procedure using flexor sublimis from the ring finger, reflected around the tendon of flexor carpi ulnaris and fixed into both the base of the first phalanx and the metacarpal bone of the thumb.

The question of amputation of an anæsthetic index may arise.

*Associated low lesions of the median and ulnar nerves* would be the best indication for transposition of flexor sublimis into the interosseous tendons. But in many of our cases concomitant lesions of the flexor muscles or tendons existed and the problems were similar to those presented by high injuries.

*High lesions.*—Irreparable lesions of the *median* in the arm are very serious. But the integrity of interosseous muscles gives reasonable chances of success to tendon transplantations. The best plan seems to be: transfer of brachioradialis into flexor profundus, extensor carpi radialis into flexor pollicis longus and the use of flexor carpi ulnaris to restore opposition. But instability of the wrist may demand arthrodesis as a second stage.

High lesions of the *ulnar nerve* are followed in almost all cases by serious trouble in the intrinsic muscles of the hand: but Bunnell's operation is only possible when flexor profundus of the ring and little fingers is working. If it is not, we prefer to deal with the claw-hand by interphalangeal arthrodesis of the ring and little fingers.

After high irreparable lesions of *both median and ulnar nerves*, the patients with their anæsthetic claw-hand showing practically no motion appear rather desperate cases. Still, something can be done but one has to limit one's ambition to restoring the gross function of pinching and grasping.

Among the various possibilities we consider the following as the safest:

Interphalangeal arthrodesis for the claw-hand, transplantation of brachioradialis into flexor profundus, of extensor carpi radialis into flexor pollicis longus, and the thumb is fixed in opposition by an intermetacarpal bone-block. But the position of fingers and thumb must be very carefully adjusted when performing the arthrodesis: otherwise the tips of the fingers will not be able to meet the thumb owing to the small range of motion gained by tendon transplantation.

Among the operations I have so briefly mentioned a sharp distinction must be made. Some of them are simple and quite safe operations which with experience can be counted on to give good results: arthrodesis of the shoulder, bone-block of the elbow, tendon transplantation for radial paralysis and, I think, very soon, Clark's operation for biceps paralysis.

On the other hand operations for paralysis of the flexors and intrinsic muscles of the hand need a very great experience and skill in both their choice and performance and should be done only in specialized hand centres.

#### A. M. Hendry, F.R.C.S. Ed.: The Flail Limb.

From a considerable experience over many years of trying measures to lessen the residual disabilities which unfortunately often persist after every means has been adopted to restore normality of function in cases of brachial plexus and other peripheral nerve lesions, or after severe soft tissue damage in the upper limb, the following opinions emerge.

(1) The variation of the paralyses in location and degree, aggravated by deformity or contractures due to gravity, fibrosis or perhaps faulty splintage, makes classification practically impossible.

(2) In every case two groups of factors must be considered: (a) The actual physical conditions present in the limb as a whole. (b) The general attributes of the patient, e.g. sex, education, previous training or occupation, adaptability for and availability of alternative employment.

It follows that each case must be assessed on its merits since obviously two cases presenting practically similar physical disabilities may have to be dealt with differently in the light of the second group of considerations. The problems, therefore, become almost as numerous as the cases themselves. The time available may thus best be spent in considering what may and can be done for the limb flail in all its parts, since, although such a limb is extremely rare—there usually being some power acting on a part of it, or capable of being transferred to useful purpose—if the retention of such a flail limb can be justified as against amputation, the more so would be the case where improvements are possible in the light of such available power.

As they are practically irretrievable, arthrodesis and other joint limiting procedures ought not to be done until it is assured that they are either essential, or, in the particular case, preferable to the mobile joint.

In this paper the order of consideration of the parts is chosen for ease of explanation and is not necessarily that in which they should be dealt with in practice.

*The elbow.*—An arm which hangs extended at the elbow can be improved if the hand can be made to project in front of the body. This can be achieved by a posterior elbow bone-block. This operation has been described elsewhere. The check to extension can be placed at any angle deemed best for the particular case. In the completely flail limb a position about the right-angle is perhaps the most useful if the hand is to be used for carrying purposes, otherwise it may with advantage be lower. The posterior bone-block is preferable to arthrodesis because from the limit of extension the forearm can be passively flexed so as to place the hand on a table or desk and to get it out of harm's way in a crowd. This is particularly important if the shoulder is to be arthrodesed.

*The shoulder.*—A posterior elbow bone-block may not ensure a forward projecting forearm when the shoulder is flail, as the weight of the forearm will tend to make it rotate across the front of the body. In some cases it is conceivable that this may not be a disadvantage but if it is, arthrodesis of the shoulder is necessary to prevent it. The arthrodesis needs to be in just such a degree of abduction, and especially of external rotation, as will ensure that the forearm clears the chest wall, but it must be remembered that the position of external rotation has to be more than seems necessary when the forearm is in contact with the chest, because of the further forward rotation of the scapula which will take place.

*The forearm and hand.*—By the combination of a posterior elbow bone-block and shoulder arthrodesis a forward projecting forearm can be achieved. The possibilities for the hand may be outlined as follows:

*Forearm in complete supination:* The hand will hang in extension at the wrist.

(a) If the position is fixed the fingers can be formed into a claw by a tenodesis of their flexors to the radius. The tension of such tenodesis depends on the mobility of the finger-joints: the more mobile the finger-joints are the greater the tension can be as by passively extending the interphalangeal joints the metacarpophalangeal joints will flex to open the claw.

(b) If the wrist is mobile, the tenodesis is best carried out with the wrist about the mid-position of the available excursion. This permits of the wrist and metacarpophalangeal joints being passively flexed to open the claw which will close upon and thus grip an object placed in it as the hand drops back into extension. Such a claw provides a broader carrying surface, capable of holding moderately sized articles, than a single hook.

(c) If the forearm is capable of being passively pronated and the wrist is mobile the extensors may be tenodesed as well, as then in pronation the tightening of the extensors as the hand drops into flexion at the wrist will open the claw. This, however, is really only of much use if pronation and supination are actively controlled.

(d) In some cases arthrodesis of the wrist in straight position may be preferable so that the palm may provide a flat surface upon which an object, e.g. writing tablet, may be rested. This can always be done even if a prior tenodesis of the flexors has been carried out. In any case a finger-joint which is or becomes contracted can be arthrodesed in better position.

*Forearm in complete pronation:* The hand will hang in flexion. By tenodesis of their flexors to the radius the fingers can be formed into a claw but the variable tensions cannot be obtained as is possible when the forearm is in supination. Apart from being able to carry a light object in the clawed fingers such a hand is of little use. It is, however, capable of alteration in a manner similar to those limbs which are in a position between pronation and supination.

*Forearm in a position between supination and pronation:* In these cases the hand tends to hang in ulnar deviation, is unsightly and very useless: the palm does not offer a supporting surface, nor can the fingers be usefully clawed. The position of the forearm in these cases, and in those which are in complete pronation, can be altered to complete supination by a cone rotational osteotomy of the radius in its upper third. The hand can then be dealt with as outlined for the supinated forearm. An arthrodesis of the wrist will be required to correct a fixed ulnar deformity, and the position of such arthrodesis will depend upon whether a finger claw or weight-carrying palm is preferred.

*The cosmetic position:* The position of the forearm and hand which gives the best appearance, which can always be achieved even after any of the preceding suggestions have been tried, and which perhaps is preferable in most women and in those of the higher educated classes and occupations where the carrying of articles is less important, is one where the



forearm is in practically mid-position. This can always be obtained by a cone rotational osteotomy of the radius in its upper third. The wrist should be arthrodesed to prevent or correct ulnar deviation, and the thumb stabilized in forward abduction by an intermetacarpal bonestrut. By this means a flat plateau is provided by the first interosseous space on which an object held in the other hand may be balanced or supported. The ulnar border of such a hand is more serviceable to steady papers on a desk and less liable to trophic sore thereby than is the fifth finger of an ulnarly deviated hand.

Many of the patients may prefer to have the shoulder mobile despite the tendency for the forearm to fall across the front of the body at rest. For this reason, as well as for the ease of performing other operations in the limb, arthrodesis of the shoulder should be the last surgical procedure carried out.

What have been described are but basic procedures in the completely flail limb. Such are, however, very rare. They are the worst that can happen short of circulatory defects leading to death of a part. Improvements from the results indicated are usually possible even if there be but one muscle capable of voluntarily activating a part: for example, a muscle that may be transferred to enable the patient at will to grip an article with his thumb against the rigid fingers, or vice versa, or to flex the elbow or push the arm forward. When the advantages or disadvantages of such limbs in comparison to amputation with subsequent prosthesis are considered it has to be remembered that small degrees of power may enable a patient to move his own limb such as it is, but may not suffice to move part of it plus a prosthesis. The challenge, however, is to justify the retention of the flail limb.

The completely flail limb dealt with as has been outlined is considered preferable to amputation for the following reasons based on considerable personal experience.

- (1) The psychological effect.
- (2) Very few upper limb amputees wear their artificial limb at all, and the majority who do only wear the gloved hand at times, so that the argument of the advantages of the special fittings loses much of its weight.
- (3) Many employers will give a patient work with such a limb who would not entertain the idea at all had he an artificial one. The claw of such a hand will, for example, bear a paint pot even more securely than a hook and such a hand will damage wall-paper less. Four such patients are house decorators.
- (4) Because of having to use the good hand chiefly it becomes the more liable to trauma and subsequently incapacity: it may become affected with poliomyelitis. What then? Should it become equally paralysed, is it to be amputated also? If not, then what is done for it might have been done for the other.

(5) Apart from that improbable occurrence if efforts to improve such limbs are not attempted what is to be done for a patient who presents two such limbs?

(6) One can always amputate. If, however, a patient tends to decline such procedures or even after them requests amputation, it is suggested that the following tests be put.

Ask him to wear a glove at all times no matter where he is, or to keep the affected limb entirely within the clothes and with the corresponding coat or dress sleeve pinned up. If the patient be a woman, ask her to keep to long-sleeved dresses, wearing a glove constantly, or to obtain a covering for her arm of any material as near to flesh colour as she imagines an artificial limb may be, and to keep it on despite the colour of her dresses. If the patient would still prefer the artificial limb, then one may amputate because only then can an orthopaedic surgeon with justice claim to have done the best he could for his patient.

#### H. J. Seddon, M.A., D.M., F.R.C.S.: Transplantation of Pectoralis Major for Paralysis of the Flexors of the Elbow.

In paralytic conditions of the upper limb loss of active flexion of the elbow is a frequent and always disabling feature, and for this reason the new operation described by J. M. P. Clark in 1946 immediately attracted attention. At that time hundreds of ex-Servicemen suffering from the effects of peripheral nerve injury had reached the stage where reconstructive surgery was required.

There is no need to repeat the full description of the operation, though a few important technical points that have emerged with increasing experience are worth mentioning. Clark's operation is applicable in cases where the lower part of pectoralis major has been spared. The lower third of the muscle is freed from the remainder and from its origin: a piece of the sheath of the rectus abdominis is elevated in continuity with the distal end of the transplant so as to serve as a tendon later in the operation. As Clark has shown so clearly the lower part of pectoralis major has a separate nerve supply (and blood-vessels), and when the dissection is being carried proximally it is convenient to seek out the position of this nerve by bipolar electrical stimulation. The dissection of the pedicle of the transplant is carried

as far proximally as possible and is the one part of the operation requiring technical finesse. The second incision in the lower third of the arm should be L-shaped, the horizontal limb lying across the line of the elbow-joint, the vertical running along the lateral margin of the biceps. In opening up a space beneath the deep fascia for the reception of the transplant it is important to ensure that the diameter of the tunnel is adequate proximally; otherwise there will be difficulty in drawing the very considerable mass of muscle down into the anterior compartment of the arm and a real danger of jeopardizing its blood supply. When the transplant is lying comfortably in its new position the correct degree of tension for suture is determined before the upper wound is closed: the neurovascular bundle, easily palpable beneath the muscle mass, must not be taut. The incision on the chest wall can then be closed; axillary drainage is not required if there is no oozing. The correct position of the elbow is flexion to 30 degrees above a right angle, and full supination of the forearm. It is usually possible to thread the aponeurotic "tail" of the transplant (the piece of rectus sheath) through the tendon of the biceps, but sometimes the *pectoralis major* is short and one then has to be content with suturing it to the underlying belly of the biceps. The elbow and forearm are immobilized for three weeks by means of a posterior plaster slab, the arm being supported in a sling.

If the programme of treatment includes arthrodesis of the shoulder this operation is best carried out before the muscle transplant, in order to avoid a long and possibly harmful period of fixation of the elbow.

*After-treatment.*—After three weeks the plaster and the stitches are removed, the sling is retained for another three weeks, the transplanted muscle is stimulated daily with a faradic current and re-education of the muscle is started. At first, flexion of the elbow is accompanied by contraction of the undisturbed part of the *pectoralis major*, but after a very variable period—six to twenty-four weeks—*independent* flexion of the elbow is achieved and with it sometimes a most gratifying range of active supination.

*Summary of cases treated and of results.*—The operation has been performed 16 times, in one case on both sides. Of the 15 patients, 2 had suffered gunshot injuries of the brachial plexus; one, a child, had had poliomyelitis; another, a child, had paralysis of the elbow flexors as a result of amyoplasia congenita, the pectorals being partly spared; the rest had suffered traction injuries of the plexus. In 4 cases where the transplant itself was subnormal in power *pectoralis minor* was used in addition. In 11 cases the flexors of the elbow were not completely paralysed, but much too weak to raise the elbow against gravity.

In 15 transplants the result was sufficiently good to justify the operation: in 7 the result was excellent, the elbow flexing powerfully against gravity and resistance: in the remainder the limb could be raised against gravity and slight resistance, that is to say, the patient had good control of the arm but not to the extent of being able to lift more than a light object.

In 7 cases supination against resistance was regained with ranges of active movement varying from 10 to 90 degrees.

(A film was shown to illustrate the operative technique and some of the results.)

#### REFERENCE

CLARK, J. M. P. (1946) *Brit. J. Surg.*, 34, 180.

Donal M. Brooks, F.R.C.S.J.: Tendon Transplantation in the Forearm and Arthrodesis of the Wrist.

Although the scope of reconstructive surgery of the paralysed upper limb is necessarily widened as a result of war, its application in more peaceful days to paralysis following poliomyelitis is considerable. Moreover, in civilian life peripheral nerve injuries of the upper limb are by no means rare and for the most part fall into three groups: traction injuries of the brachial plexus; nerve lesions complicating fractures; and nerve lesions occurring as a complication of lacerations and incised wounds of the forearm and hand.

Ideas about tendon transplantation have never been lacking, but with the exception of the operation for radial paralysis, few series of results have been published. The observations that follow are based on experience gained in performing such operations for residual paralysis from poliomyelitis, and in particular on a review of 287 tendon transplants in the forearm and hand performed on 145 patients who passed through the Peripheral Nerve Injuries Unit at Oxford and later at the Institute of Orthopaedics, London.

*Operative technique.*—The greatest respect must be paid to the tissues, and gentleness should equal that required in peripheral nerve surgery. General anaesthesia is best but on occasions local anaesthesia has distinct advantages when determining the correct tension at which to suture in flexor tendon transplants. A pneumatic tourniquet is used, but if the

vascular state of the limb is already impoverished by damage to a main vessel local infiltration of 1/200,000 adrenaline in saline gives satisfactory hæmostasis without subsequent ill-effects: as in plastic surgery absolute hæmostasis is essential.

The incision is so planned that the skin scar does not overlie the suture line and this means employing a curved incision with elevation of a skin flap (figs. 1 and 2). There is no place

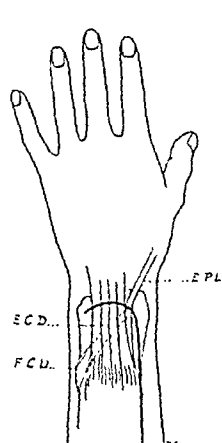


FIG. 1.—Incision used for extensor tendons.

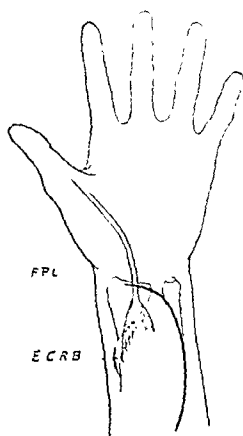


FIG. 2.—Incision used for flexor tendons.

- E.C.D. Extensor communis digitorum.
- F.C.U. Flexor carpi ulnaris.
- E.P.L. Extensor pollicis longus.
- F.P.L. Flexor pollicis longus.
- E.C.R.B. Extensor carpi radialis brevis.

for short incisions; inadequate exposure means inadequate mobilization of the motor tendon. In this review flexor carpi ulnaris was found to be the tendon most commonly employed (Table I), and it is a muscle that cannot be freed with certainty through any

TABLE I.—SHOWING RELATIVE FREQUENCY OF MOTOR TENDONS USED

| Motor tendon | Times used |    |    |    |    |    |    |    |
|--------------|------------|----|----|----|----|----|----|----|
| F.C.U.       | ..         | .. | .. | .. | .. | .. | .. | 90 |
| P.R.T.       | ..         | .. | .. | .. | .. | .. | .. | 46 |
| P.L.         | ..         | .. | .. | .. | .. | .. | .. | 43 |
| F.C.R.       | ..         | .. | .. | .. | .. | .. | .. | 43 |
| B.R.         | ..         | .. | .. | .. | .. | .. | .. | 14 |
| E.C.R.L.     | ..         | .. | .. | .. | .. | .. | .. | 14 |
| E.C.R.B.     | ..         | .. | .. | .. | .. | .. | .. | 14 |
| E.C.U.       | ..         | .. | .. | .. | .. | .. | .. | 5  |
| F.D.S.       | ..         | .. | .. | .. | .. | .. | .. | 8  |
| F.D.P.       | ..         | .. | .. | .. | .. | .. | .. | 6  |
| F.P.L.       | ..         | .. | .. | .. | .. | .. | .. | 2  |
| F.P.B.       | ..         | .. | .. | .. | .. | .. | .. | 1  |
| E.I.         | ..         | .. | .. | .. | .. | .. | .. | 1  |
| Total        | 287        |    |    |    |    |    |    |    |

but a long incision. The motor tendon lies superficial to the deep fascia where it can freely expand during contraction. The opening in the deep fascia through which the motor tendon passes to the recipient tendon is large in order to prevent adhesions occurring. In extensor transplants the distal part of the extensor retinaculum is preserved so that "bow-stringing" of the tendons is avoided. Fine black silk is used for suture; no deep sutures are inserted and after skin closure the limb is immobilized in plaster of Paris in the position of maximum relaxation for the transplant. For this reason simultaneous flexor and extensor transplants should be avoided. For the first five days at least the patient is strictly confined to bed and the limb elevated. At the end of three weeks, during which time no attempt at movement is made, the plaster and stitches are removed, and a back slab is worn for decreasing periods during the next two weeks.

*Re-education.*—During re-education some knowledge of the operation is useful to the patient and essential to the physiotherapist. Faradism to the muscle belly of the transplant is often disappointing in the early stages whereas attempting the normal action of the motor tendon can be quickly associated with the new movement. Massage to the scars promotes

as far proximally as possible and is the one part of the operation requiring technical finesse. The second incision in the lower third of the arm should be L-shaped, the horizontal limb lying across the line of the elbow-joint, the vertical running along the lateral margin of the biceps. In opening up a space beneath the deep fascia for the reception of the transplant it is important to ensure that the diameter of the tunnel is adequate proximally: otherwise there will be difficulty in drawing the very considerable mass of muscle down into the anterior compartment of the arm and a real danger of jeopardizing its blood supply. When the transplant is lying comfortably in its new position the correct degree of tension for suture is determined before the upper wound is closed: the neurovascular bundle, easily palpable beneath the muscle mass, must not be taut. The incision on the chest wall can then be closed; axillary drainage is not required if there is no oozing. The correct position of the elbow is flexion to 30 degrees above a right angle, and full supination of the forearm. It is usually possible to thread the aponeurotic "tail" of the transplant (the piece of rectus sheath) through the tendon of the biceps, but sometimes the pectoralis major is short and one then has to be content with suturing it to the underlying belly of the biceps. The elbow and forearm are immobilized for three weeks by means of a posterior plaster slab, the arm being supported in a sling.

If the programme of treatment includes arthrodesis of the shoulder this operation is best carried out before the muscle transplant, in order to avoid a long and possibly harmful period of fixation of the elbow.

*After-treatment.*—After three weeks the plaster and the stitches are removed, the sling is retained for another three weeks, the transplanted muscle is stimulated daily with a faradic current and re-education of the muscle is started. At first, flexion of the elbow is accompanied by contraction of the undisturbed part of the pectoralis major, but after a very variable period—six to twenty-four weeks—-independent flexion of the elbow is achieved and with it sometimes a most gratifying range of active supination.

*Summary of cases treated and of results.*—The operation has been performed 16 times, in one case on both sides. Of the 15 patients, 2 had suffered gunshot injuries of the brachial plexus; one, a child, had had poliomyelitis; another, a child, had paralysis of the elbow flexors as a result of amyoplasia congenita, the pectorals being partly spared; the rest had suffered traction injuries of the plexus. In 4 cases where the transplant itself was sub-normal in power pectoralis minor was used in addition. In 11 cases the flexors of the elbow were not completely paralysed, but much too weak to raise the elbow against gravity.

In 15 transplants the result was sufficiently good to justify the operation: in 7 the result was excellent, the elbow flexing powerfully against gravity and resistance: in the remainder the limb could be raised against gravity and slight resistance, that is to say, the patient had good control of the arm but not to the extent of being able to lift more than a light object.

In 7 cases supination against resistance was regained with ranges of active movement varying from 10 to 90 degrees.

(A film was shown to illustrate the operative technique and some of the results.)

#### REFERENCE

CLARK, J. M. P. (1946) *Brit. J. Surg.*, 34, 180.

#### Donal M. Brooks, F.R.C.S.I.: Tendon Transplantation in the Forearm and Arthrodesis of the Wrist.

Although the scope of reconstructive surgery of the paralysed upper limb is necessarily widened as a result of war, its application in more peaceful days to paralysis following poliomyelitis is considerable. Moreover, in civilian life peripheral nerve injuries of the upper limb are by no means rare and for the most part fall into three groups: traction injuries of the brachial plexus; nerve lesions complicating fractures; and nerve lesions occurring as a complication of lacerations and incised wounds of the forearm and hand.

Ideas about tendon transplantation have never been lacking, but with the exception of the operation for radial paralysis, few series of results have been published. The observations that follow are based on experience gained in performing such operations for residual paralysis from poliomyelitis, and in particular on a review of 287 tendon transplants in the forearm and hand performed on 145 patients who passed through the Peripheral Nerve Injuries Unit at Oxford and later at the Institute of Orthopaedics, London.

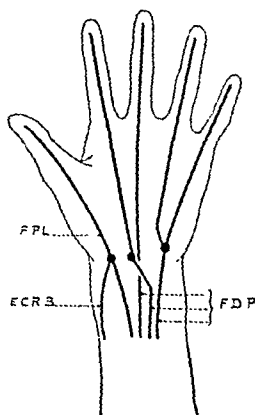
*Operative technique.*—The greatest respect must be paid to the tissues, and gentleness should equal that required in peripheral nerve surgery. General anaesthesia is best but on occasions local anaesthesia has distinct advantages when determining the correct tension at which to suture in flexor tendon transplants. A pneumatic tourniquet is used, but if the

Secondly, employing palmaris longus and brachioradialis—both muscles with a limited traverse—as motor tendons. Function was disappointing, the former being too weak, and the latter too powerful, and the range of movement of both unsatisfactory.

Thirdly, in a few cases in which flexor carpi radialis was not paralysed it was buttonholed through the long flexors, and of the three methods this gave the most satisfactory function though naturally the range of movement was somewhat limited and no independent movement was possible. If in these transplants the motor tendon was simultaneously passed through the superficial and deep tendons the results were rather worse; it is better to transplant it into the deep flexors alone.

In the transplant that is now used one employs the short radial extensor as the motor tendon for the long flexor of the thumb, and the deep flexor of the ring finger for deep flexor of the index (fig. 3). The traverse of extensor carpi radialis brevis enables the thumb to be flexed through a full range of movement and the traverse of the deep tendons is of course identical.

For thenar paralysis, palmaris longus was used at first as the motor tendon for active abduction and opposition of the thumb. The correct line of action was obtained by detaching the tendon of extensor pollicis brevis from its muscle belly and passing it subcutaneously across the palm towards the pisiform where it was united to palmaris longus which had been passed around the distal portion of the tendon of flexor carpi ulnaris, as suggested by Bunnell (1944). The results were seldom successful for the following reasons; Firstly, the tendon suture, situated in an area where subcutaneous fat is sparse, often becomes adherent. Secondly, in fashioning a pulley by passing the tendon of palmaris longus around flexor carpi ulnaris, the deep fascia is pierced twice and adhesions often occur at these points. Thirdly, as emphasized before, palmaris longus has a very limited traverse. If, however, extensor carpi ulnaris is used as the motor tendon (fig. 4) a satisfactory action can be obtained



- F.P.L. Flexor pollicis longus.  
E.C.R.B. Extensor carpi radialis brevis.  
F.D.P. Flexor digitorum profundus.

FIG. 3.—Showing transplant employed for paralysis of F.P.L. and F.D.P. to index.



FIG. 4.—Showing active opposition of thumb [following transplantation of E.C.U. into E.P.B. where no pulley was used.

and no pulley is required. This type of transplant has now been superseded where possible by using the sublimis tendon of the ring finger as the motor tendon and inserting it directly into bone on the outer aspect of the base of the proximal phalanx of the thumb. The correct line of action can be obtained either by fashioning a loop on the superficial aspect of the tendon of flexor carpi ulnaris (Irwin, 1942) or more simply by passing it distal to the carpal tunnel to its point of insertion. Good results have been seen with both methods; the most important factor is that a tendon junction in the subcutaneous tissues is avoided.

*Ulnar nerve.*—In ulnar paralysis the disability is sometimes not very great but if acute

mobility and prevents adhesions. Re-education is carried out twice daily for the first week, then once a day for a further two or three weeks; thereafter an early return to work is encouraged so that the limb can be used naturally. The degree of dissociation of movement that can take place in a motor tendon after transplantation was well demonstrated by Zachary (1946), who failed to detect action potentials in flexor carpi ulnaris on active flexion of the wrist, when it had been transplanted into the extensors of the fingers, in a case of radial paralysis.

#### TENDON TRANSPLANTATION FOR INDIVIDUAL NERVE PARALYSIS

Of the 145 patients in which tendon transplantation for forearm paralysis was performed most of the operations—109—were extensor transplants following lesions involving the whole or part of the radial nerve distribution. 24 operations were for long flexor paralysis and a further 12 for paralysis of the small muscles of the hand (Table II).

TABLE II.—ANALYSIS OF TENDON TRANSPLANTS IN THE FOREARM

| Paralysis              | Nerve           | No. of cases |
|------------------------|-----------------|--------------|
| Forearm extensors      | Brachial plexus | 12           |
|                        | Radial          | 48           |
|                        | Post. Int.      | 30           |
|                        | Partial lesions | 19           |
| Long flexors of digits | Median          | 24           |
| Thenar muscles         | Median          | 6            |
| Interossei             | Ulnar           | 6            |
| Total                  |                 | 145          |

*Radial Nerve.*—In the classical operation for radial paralysis (Jones, 1917), pronator teres is buttonholed into the radial extensors, flexor carpi radialis into the extensors of the thumb and long abductor, and flexor carpi ulnaris into the remaining extensors of the digits. Slight variations have been adopted from time to time but there is general agreement that so far as dorsiflexion of the wrist is concerned pronator teres is an effective motor tendon.

In the earlier cases of this series the classical method was used but it was soon apparent that although the technique was uniform the results were variable. In some cases active extension of the digits was accompanied by acute dorsiflexion of the wrist and imperfect extension of the metacarpophalangeal joints. In active extension of the digits the wrist normally assumes the neutral position or becomes slightly palmar flexed, the exact opposite, in fact, to the position assumed in gripping. Simultaneous active extension of the wrist and digits is a movement rarely employed. The good results in these earlier cases were found to be those in which palmaris longus was present and working strongly. Moreover, in those cases in which dorsiflexion of the wrist occurred with extension of the digits, if the wrist was stabilized in the neutral position full metacarpophalangeal extension took place. Thus Zachary (1946) emphasized the importance of retaining flexor carpi radialis as a strong wrist flexor and using palmaris longus for the thumb tendons. This improved the results considerably; so far as the fingers were concerned the action became almost perfect. Full palmar abduction of the thumb as in grasping was still often defective. But this is not surprising, for a single motor tendon was expected to perform two distinct movements normally carried out by the long extensor and long abductor of the thumb.

A further modification was therefore incorporated and flexor carpi ulnaris was used to extend the thumb as well as the fingers (fig. 1), palmaris longus being employed for the short extensor and long abductor. If palmaris longus is absent flexor carpi ulnaris must, of necessity, be transplanted into all the extensor tendons and the long abductor of the thumb. It sometimes happens that radial deviation of the wrist occurs at rest and on active extension owing to the loss of muscle balance on the ulnar side; in these cases a secondary transplant of one or both of the radial extensors into extensor carpi ulnaris has resulted in an almost normal action of the wrist. In posterior interosseous palsy the transplant is similar except for the omission of pronator teres as a wrist extensor.

*Median nerve.*—The main disability in paralysis of the long flexors innervated by the median nerve is loss of flexion of the index and thumb; the middle finger is seldom seriously affected as it often gains a passive pull from the deep tendons of the ring and little fingers. In the earlier cases with this paralysis three procedures were tried:

Firstly, lateral hitching of the paralysed tendon to its adjacent unparalysed comrade—for example, hitching the deep tendon of the index to the deep tendon of the ring finger; without exception the results were poor.

mented by the addition of iliac chips to form a buttress on the medial side; however in the 6 cases where this modification was employed, it was found that no time had been saved.

So far there has been only one objection to this operation. Pronation of the forearm is achieved by the action of brachioradialis from full supination to mid-position and by that of pronator teres and pronator quadratus throughout the whole range of movement. In lesions of cervical 5, 6 and 7, and in some cases of poliomyelitis, pronator quadratus is the only active pronator left and in excision of the distal end of the ulna its action is inevitably destroyed. This is a real disadvantage and one not overcome by the long flexors of the fingers; the radio-ulnar joints are in fact flail. In one case flexor carpi ulnaris was passed around the radial border of the forearm on its way to the extensors of the fingers in an attempt to provide a pronator action, but the muscle was of inadequate strength after transplantation though technically there were no difficulties. In the most recent case the inferior radio-ulnar joint was fused in a position of slight pronation and a tibial graft inserted in the radiocarpal joint through a postero-radial incision.

It is possible that by a future modification of the Smith-Petersen operation whereby fusion of the ulna and radius in a position of slight pronation is achieved, this one disadvantage of an otherwise excellent operation will be overcome.

#### REFERENCES

- BUNNELL, S. (1944) *Surgery of the Hand*. Philadelphia.  
 IRWIN, C. E. (1942) *Sth. med. J.*, 35, 257.  
 JONES, R. (1917) *Notes on Military Orthopaedics*. London.  
 SEDDON, H. J. (1946) Personal Communication.  
 SMITH-PETERSEN, M. N. (1940) *J. Bone Jr. Surg.*, 22, 122.  
 STILES, H. J., and FORRESTER-BROWN, M. F. (1922) *Treatment of Injuries of the Peripheral Spinal Nerves*. London.  
 ZACHARY, R. B. (1946) *Brit. J. Surg.*, 33, 358.

**Mr. F. G. St. Clair Strange:** In spite of the apparently general acceptance of the feasibility of performing tendon transplantation, in cases such as radial palsy, after arthrodesis, I am not certain that this is correct, and have personally preferred to perform the transplant first. The reason is that after arthrodesis, the muscles to be used as motors have had a prolonged period of immobilization, and have therefore largely lost their function. I have gained the impression that re-education of these muscles when transplantation has been performed after arthrodesis is more difficult and more prolonged than where it has been performed before.

**Mr. K. I. Nissen:** The swelling of the soft tissues after arthrodesis of the wrist is often considerable and may require splitting even of a well-padded cast. The oedema about the wrist does not favour early return of function in any tendons transplanted at this time.

**Mr. A. S. Blundell Bankart:** The completely anaesthetic hand is useless, and I suggest that sensory loss may be as important as motor paralysis in determining the treatment of the severely paralysed limb.

**Mr. J. M. P. Clark (Leeds):** Two points in the technique of the pectoral transplant operation have been mentioned, one in regard to the fixation of the transplant and one in regard to the localization of the nerve supply of the transplant.

It has not always been possible to make the transplant extend as far as the tendon of the biceps and in those patients the transplant, after being threaded through the muscle belly of the biceps at the most distal point possible, must be securely sutured to the biceps muscle. There is no evidence yet available that the power of the new biceps is thereby reduced nor has there been reported any instance of the transplant's pulling adrift.

The nerve supply to the pectoral transplant is the medial anterior thoracic nerve and it is usually found quite easily when the transplant is stripped up from the ribs. Because of the possibility of anatomical variation the localization of the medial anterior thoracic nerve has been investigated and invariably the nerve issues from the pectoralis minor at a point on a perpendicular dropped from the coracoid process where it crosses the third rib and then the nerve pierces the pectoralis major near its lower border. A strip of pectoralis major wide enough to form a suitable transplant will inevitably include the nerve.

**Mr. W. D. Coltart:** I should like to ask the speakers whether they still use the opponens graft in the treatment of paralysis of the thumb.

**Mr. Norman Capener:** (a) When arthrodesis of the shoulder is carried out for a limb with weak elbow flexors or after a muscle transposition operation to replace paralysed elbow flexors it is an advantage to place the shoulder in a few degrees internal rotation, for when the limb is abducted by thoraco-scapular motion, the weight of the forearm initiates the flexion movement automatically from full extension.

hyperextension of the metacarpophalangeal joints occurs on active extension of the fingers it becomes virtually impossible to pick up anything from a flat surface. If when this hyperextension is controlled by an ulnar splint of the "knuckle-duster" type it is found that interphalangeal extension is possible, then tendon transplantation is likely to give a satisfactory result. Transplantation should not be considered if there is contracture of the long flexors and unless no overstretching of the extensor mechanism in the fingers has occurred as shown by the ability to extend the interphalangeal joints when hyperextension of the metacarpophalangeal joints is prevented. The transplant that has been used with success in a small number of cases is similar to that advocated by Stiles and Forrester-Brown (1922) and modified by Bunnell (1944). Flexor digitorum sublimis is detached from its insertion, withdrawn into the palm, split into its two components and each half passed distally on either side of the finger and attached to the extensor expansion. This transplant, by controlling hyperextension of the metacarpophalangeal joint, mimics the action of a "knuckle-duster" splint; the results have been very encouraging.

The other disability seen in ulnar paralysis is due to loss of active abduction of the index finger; extensor indicis has been transplanted into the first dorsal interosseous with success sufficient to warrant further trial of the operation.

#### ARTHRODESIS OF THE WRIST COMBINED WITH TENDON TRANSPLANTATION

In cases in which there is combined median and ulnar paralysis, and in poliomyelitis where there is extensive paralysis in the forearm, fusion of the wrist-joint becomes an important preliminary step whereby the muscles controlling this joint may be liberated for transplantation.

An analysis of 25 such cases (Table III) in which arthrodesis of the wrist was performed

TABLE III.—ARTHRODESIS OF THE WRIST AND TENDON TRANSPLANTATION

| Nerve                              |    |    |    |    |    | No. of cases |
|------------------------------------|----|----|----|----|----|--------------|
| Traction lesion of brachial plexus | .. | .. | .. | .. | .. | 12           |
| Gun shot wound of brachial plexus  | .. | .. | .. | .. | .. | 2            |
| Median, ulnar, radial              | .. | .. | .. | .. | .. | 4            |
| Median and ulnar                   | .. | .. | .. | .. | .. | 3            |
| Radial                             | .. | .. | .. | .. | .. | 4            |
| Total                              |    |    |    |    |    | 25           |

shows that in 12 the operation was performed as part of the treatment of paralysis due to traction injury of the roots of cervical 5, 6 and 7.

The forearm paralysis following such injuries results in a loss of action not only of the radial extensors but in addition flexor carpi radialis and pronator teres are either paralysed or very weak. The usual transplant for radial paralysis cannot be employed; preliminary fusion of the wrist-joint is necessary. At least ten methods of fusing this joint have been described and with one notable exception a dorsal incision is used, the extensor retinaculum divided, and the extensor tendons dislocated. The radiocarpal and intercarpal joints are excised always, the carpometacarpal joints sometimes. A dorsal inlay or onlay graft taken from tibia, rib or iliac crest is often employed. Where tendon transplantation is subsequently contemplated this approach has obvious disadvantages not only in the position of the scar but also in the ill-treatment of the extensor tendons and retinaculum.

In 1940 Smith-Petersen described a medial approach to this joint by excision of the distal four centimetres of the ulna. The radiocarpal joint was excised and the carpus and distal end of the radius were split transversely, a graft consisting of the excised portion of the ulna being inserted into the gap. This approach removed all the objections to other methods and appeared to be ideal for cases in which tendon transplantation was subsequently necessary. In the first 12 of this series of cases this method was used and without exception a solid fusion was obtained in an average of three and a half months. But in this approach excision of the radiocarpal joint on the radial side is difficult and the wrist becomes thickened as a result of splitting the carpus and radius. In 1946 Seddon modified the operation; he resected a triangular wedge from the lower end of the radius and a similar wedge from the carpus leaving a diamond-shaped cavity. The excised piece of ulna was then cut to form a triangle; thus when the triangle was inserted in the diamond cavity with the apex downwards, automatic dorsiflexion of the wrist of about 20 degrees occurred. This method was employed in a further 4 cases and again fusion occurred with an average period of fixation of three and a half months. In an attempt to shorten this period the grafting was supple-



## Section of Endocrinology

President—H. GARDINER HILL, M.B.E., M.D., F.R.C.P.

[March 23, 1949]

### Radon Implantation for Acromegaly and Cushing's Syndrome

By D. W. C. NORTHFIELD, M.S.

I PROPOSE to relate the results of implantation of radon in five patients, comprising 4 cases of pituitary basophilism and one of acromegaly. In one case of basophilism the result was dramatically successful, and in another there was some improvement; in a third there has been no significant benefit; the fourth case of basophilism and the case of acromegaly ended fatally.

So far as I am aware, radon implantation for pituitary basophilism was first performed in 1935 by the late Mr. Pattison, neurosurgeon at Newcastle, and Sir Hugh Cairns implanted radon seeds into the pituitary gland of a patient with basophilism at the London Hospital in 1936. The cases to be described have occurred since 1940, and I will briefly summarize the clinical records in chronological sequence; Dr. A. C. Crooke has seen all the patients and I am grateful to him for his advice and help.

I.—M. F., married woman aged 31 years, was referred by Professor Arthur Ellis in September 1940. Great increase of weight followed the birth of her only child one year previously—from 9 st. 8 lb. to 13 st. 5 lb., a gain of approximately 4 st. Blue streaks appeared in the skin of the abdomen



(A)



(B)

FIG. 1 (Case I, M. F.).—(A) Pre-operative; (B) two weeks post-operative.

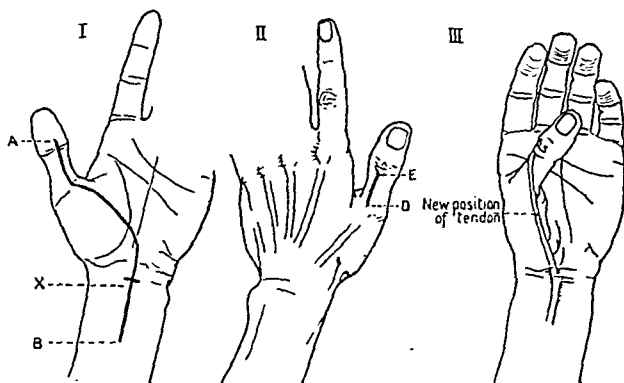
and limbs; she became dyspnoeic; her legs and back ached, the legs "gave way" on occasion after exertion; there were occasional mild headaches. During the previous nine months she had noticed increasing growth of hair on upper lip, limbs and pubes, and a heightened colour of her face. She perspired excessively. The baby born in April 1939 had been breast fed for four months when lactation ceased, but the menstrual periods did not start again until April 1940, and continued until July but then ceased again. There was no disturbance of vision, appetite, or fluid balance, and no

(b) There had been a tendency to place a bail graft too distally in operation for arthrodesis of the first metacarpal in opposition. If, however, surgeons were prepared to divide the radial artery, a much more thorough arthrodesis could be achieved at the angle between the first and second metacarpals, combining the interosseus grafts with efficient excision of the carpometacarpal joint.

**B. Whitchurch<sup>1</sup> Howell, F.R.C.S.: Operation for Opponens Paralysis of the Thumb.<sup>1</sup>**

This operation was devised by me some years ago to improve the function of a thumb in which opposition was impossible, either on account of irreparable damage to the median nerve or permanent paralysis due to anterior poliomyelitis. The operation is, in brief, a transposition of the tendon of the flexor longus pollicis performed in the following manner.

An incision, A B, is made, extending from the ball of the thumb to several inches above the transverse creases of the wrist, and the tendon isolated (I). A second incision, E D, is then made over the dorsal aspect of the first phalanx of the thumb, well to the ulnar side (II). The flap, A B, is then freely and carefully undercut towards the radial border of the thenar eminence. The tendon is then divided at the wrist at x and the distal end passed subcutaneously round the ulnar border of the first phalanx and out through the incision E D.



Next the tendon is passed back again through this incision, passing obliquely across the tendon of the extensor longus pollicis, and comes to lie subcutaneously on the thenar eminence. The fashioning of the subcutaneous tunnel is much facilitated by the use of the old-fashioned hernia needle on a handle (III). The incision E D is then sewn up; also incision A B with the exception of the part near x. At this stage the thumb is held in opposition with the terminal joint of the thumb extended. The distal and proximal ends of the tendon are then united at x with chromicized catgut (20-day) and the skin closed (III). The thumb is kept in opposition by means of plaster of Paris, a window being cut for the wound A B. Graduated faradic stimulation of the flexor longus pollicis is commenced on the fourth day, and the stitches are removed on the tenth. Within two to three months strong sustained voluntary opposition of the thumb is effected by the transposed tendon.

This operation is a transposition and not a transplantation into another tendon.

Some of the contra-indications to the operation are weakness of the flexor longus pollicis, and deformity of neighbouring joints, &c.

Hence in the treatment of this paralysis in its acute stage and for some time afterwards the position of opposition must be maintained to prevent bony deformity, and the flexor longus pollicis must be hypertrophied by faradism.

<sup>1</sup>Reprinted from the *Lancet*, 1926 (i), 131.

The face is a healthy pink, with no abnormal growth of hair on face or trunk, and rather scanty scalp hair. Fundi healthy. B.P. 110/90.



FIG. 3 (Case I, M. F.).—Nine years post-operative.

II.—E. R., a married woman aged 37 years, was admitted to the London Hospital under Dr. Clarke-Kennedy on 1.1.42. For six years there had been an increasing growth of dark hair on the chin and face; her periods stopped two and a half years before admission; nine months later she had a prolonged and sudden attack of vertigo ending apparently in unconsciousness. Details of this period of her illness are scanty, but she remained confined to bed for about three months, not because

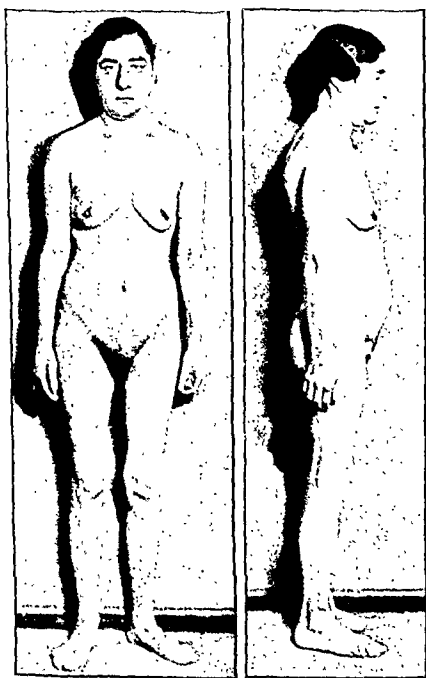


FIG. 4 (Case II, E. R.).—Pre-operative.

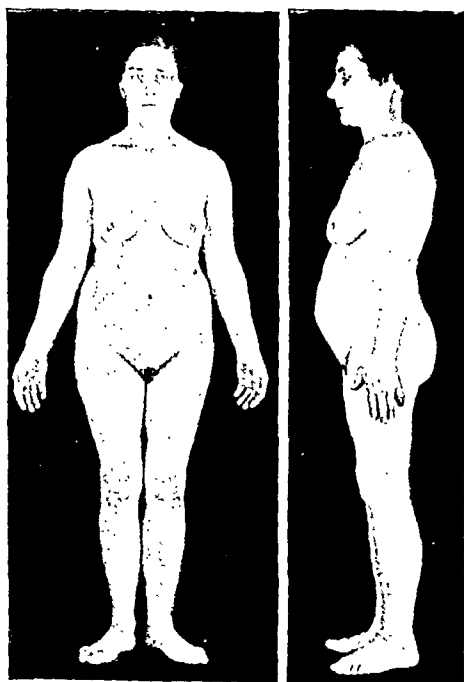


FIG. 5 (Case II, E. R.).—Seven years post-operative

nausea or vomiting. There were no previous illnesses of note. On examination she was very obese with conspicuous purple striæ atrophicæ. The face was bloated and bluish red, there was a moderate moustache but no notable hirsuties elsewhere. She was intelligent and alert and the nervous system was normal; fundi healthy, visual fields and acuity normal. The blood-pressure when first seen several months earlier was 150/70, and later it was 120/80. The skull was radiographically normal. The renal function and the blood-count were normal, the sugar tolerance curve was somewhat increased. Peri-renal air insufflation was normal. Urinary ketosteroids were 18.5 mg. in twenty-four hours. While under Professor Ellis's care she was given œstrin, and deep X-ray therapy (1,000 r), without benefit.

Operation was carried out on October 14, 1940, two radon seeds being inserted into the pituitary gland, one either side of its stalk, the total dose being 3.0 m.c. A minute fragment of tissue exuded from one of the holes made to receive the radon; this was sent for histological examination. Dr. J. G. Greenfield reported:

Sections show an adenoma of the pars anterior hypophysis, composed of rather large cells, some of which are based on the adventitia of the blood-vessels and are irregularly cuboidal in shape, but most are massed irregularly together. Their cytoplasm is fairly granular and stains blue with Mallory's connective tissue stain but also contains a varying number of more definite granules which

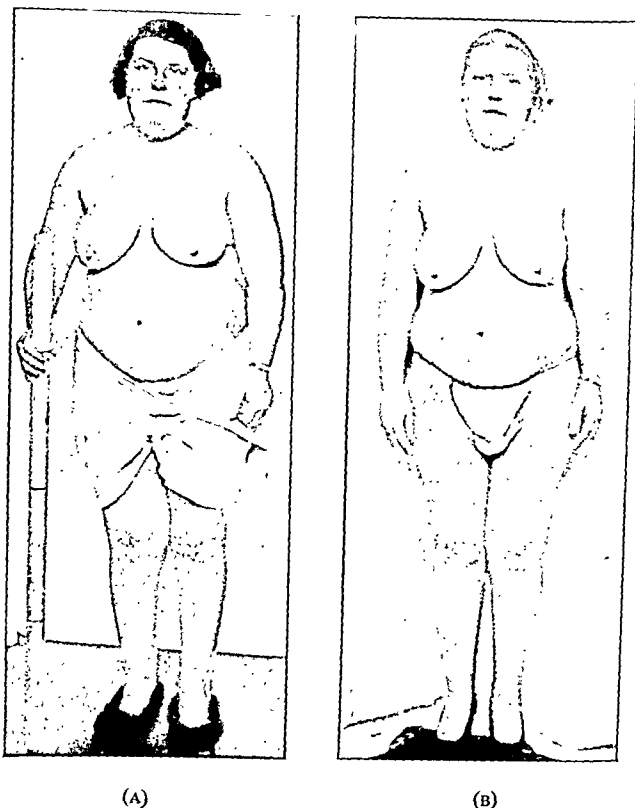


FIG. 2 (Case I, M. F.).—(A) Pre-operative; (B) two weeks post-operative.

stain with acid fuchsin. The cells have not the regular palisade arrangement usually seen in basophil adenomas, nor have they definite basophil granules. But these anomalies may be accounted for by conditions of removal and fixation.

Within a few days of the operation, there was a noticeable change in the complexion, and by the ninth day this had become dramatic, for the skin of the face was peeling like a case of scarlet fever. In the first sixteen days after the operation she lost 19 lb. and she continued to lose weight steadily, reaching 10 st. about one year later though since then it has fluctuated. During the first few months of convalescence she was troubled with much muscular weakness and lassitude which gradually passed. The menses recommenced three months after the operation and were regular for about two years, then ceasing. The complexion became quite clear, the skin a rather youthful healthy pink, and the moustache disappeared practically completely. When last seen on March 18, 1949, she looked well, weighing 11 st. 11½ lb., complained still of fatigability and some headache. No polydipsia.

hair was of male distribution. The fundi could not be seen clearly, the visual fields showed evidence of chiasmal compression—a relative temporal hemianopia of the smaller isopters in the right eye with a central scotoma on both sides, visual acuity right and left 6/60. Radiography: marked enlargement of the sella (fig. 6). Renal function normal. Although she was under regular observation and taking the recommended doses of insulin, the diabetes proved very difficult to control; on account of this and the ocular diabetic manifestations radon implantation was decided upon. Dr. C. A. Birch gave valuable advice concerning the diabetes, and on April 28, 1943, the pituitary was exposed through a right frontal craniotomy. A large frontal sinus made the approach awkward, and the tip of the frontal lobe had to be removed. The chiasma was prefixed, making manipulations more difficult owing to poor access. The tumour was causing a bulge between the nerves, and on nicking its capsule in order to insert the radon, there was an immediate spontaneous evacuation of soft tumour tissue which was highly vascular. In order to control bleeding much of the tumour had to be sucked out, as one does ordinarily for a pituitary adenoma. When bleeding had been fully controlled, 6 radon needles totalling 9 m.c. were inserted into the sella. Her condition deteriorated some hours after the operation and the wound was opened up to disclose great oedema of the brain and some clot in the vicinity of the sella; the clot was removed and a wide decompression performed. Nevertheless, she died the next day. Post-mortem revealed a much more extensive tumour than was suspected. There was a central mass  $2.5 \times 2$  cm. in the sella, with a lobule  $2 \times 1.7$  cm. pressing up into the floor of the third ventricle, and another lobule which had burst through the lateral wall of the cavernous sinus to form a mass indenting the inner aspect of the right temporal lobe. Histologically the tumour was a very cellular and vascular eosinophilic adenoma.

IV.—D. L., a married woman of 37 years, was referred to me by the Medical Superintendent of Essex County Hospital, Wanstead, in October 1944. Since her baby had been born eighteen years previously she had slowly increased in weight, and become unduly tired and breathless on exertion. For two years the increase in weight had been more marked, hair had grown excessively on the chin and lips, and there had been attacks of falling, headaches, backache and thirstiness; later some impairment of vision, and attacks of giddiness developed. The menses were regular, though becoming scanty.

*On examination.*—Gross obesity of trunk and proximal parts of limbs (weight 16 st. 7 lb.; height 4 ft. 8 in.) florid complexion, slight moustache and beard, no hirsuties of limbs or trunk, moderate upper thoracic kyphosis. Blood-pressure 185/115. No abnormality of nervous system; optic fundi and fields normal. Renal function and glucose tolerance tests normal; some polyuria. Urinary 17-ketosteroids 13.2 mg. per twenty-four hours. It was decided that deep X-ray treatment should be given, and this was carried out under the supervision of Dr. Frank Ellis at the London Hospital between December 1944 and May 1945. The only significant improvement was in the menses. Her weight remained about the same, but the hairiness of her face, and the bloated complexion, seemed somewhat worse. Radon implantation was decided upon, and operation was attempted on June 13, 1946. Owing to excessive bleeding and an engorged and tight brain, the procedure was abandoned after the reflection of the bone flap and the wound thereupon closed. Recovery was stormy, and the wound became infected but ultimately healed satisfactorily. Six months later, on January 21, 1947, a further operative attempt was made, her headaches having increased and being associated with vomiting. One radon seed containing 1.1 m.c. was satisfactorily inserted into the pituitary and she made an uncomplicated recovery. On the fourth post-operative day there was slight peeling of the skin of the face, as described in the first case. The blood-pressure three months after operation was 130/90 compared with 180/100 before, though when seen two months ago it had risen to 175/125. She is a little less fat (15 st. 10 lb.) and the colour of the face has improved. The hairiness of her face has diminished so that she now shaves once in two months. She has much less headache and vomiting, and is generally more cheerful and interested in activities around. She occasionally menstruates.

V.—B. S., single woman aged 30, was referred by Dr. Leonard Simpson and I am grateful to him for details concerning her previous records. She had been sent to Dr. Simpson in February 1947 from Palestine because treatment there had given no relief. Five years previously she began to grow excess



1937



1942



1946

FIG. 7 (Case V, B. S.).—Showing development of characteristic facies.

of paralysis, but because of great lassitude. From this time she gave up her household and outside work. She took no interest in her family and her thoughts centred only on her worries and miseries; she became profoundly depressed. She visited many doctors, and eventually she was persuaded to attend hospital. She had headaches, backache, excess sweating and some nocturnal frequency of micturition. She lost weight—2 st. in two years—and had no interest in food; there was no disturbance of vision. On examination she was a thin, dejected woman, readily bursting into tears. Face and nose were red and covered with many venules; there was a marked moustache and beard, moderate hirsuties over trunk, and a male distribution of pubic hair; skin greasy and coarse with hæmorrhagic rash over trunk and numerous bruises were present, apparently spontaneous; slight swelling of thyroid isthmus. Visual fields and acuity were normal, as was the rest of the nervous system. Blood-pressure 150/100; 135/75. Slight dorsal kyphosis. Fluid balance, renal function, blood-count and bleeding time normal; occasionally a trace of albuminuria. She was seen by Dr. Henry Wilson because of her mental state, who found her properly orientated and sensible, with insight, but completely preoccupied with her depression, her physical appearance and her lethargy. He considered that if the physical condition were not cured, she would become an inmate of a chronic mental institution. Mr. Alan Perry performed a laparotomy to exclude a suprarenal tumour. On February 24, 1942, two radon seeds were inserted in the pituitary gland, the total dosage being 3.7 m.c. Her recovery from operation was slow and there was not the dramatic change in the face which occurred in the previous patient, but a definite improvement was noticeable after about five weeks when she left hospital.

Her mental state only slowly improved. Her menses returned six months after operation, and persisted regularly though excessively for eighteen months and then ceased. At the present time, seven years after the operation, she is cheerful and working hard, looking after her husband who is crippled with disseminated sclerosis, and working outside the home two half-days a week. The colour of the face is normal though the venules are still present and the skin is not greasy; she shaves alternate days though I doubt if this is necessary. Sweats occur occasionally. Blood-pressure 120/90. Weight 10 st.

III.—G. F., a single woman aged 30 years, had been attending the Diabetic Clinic at the London Hospital for five years, prior to her transfer to my care in 1943. Increase of hair on the face and body had been noticed for ten years, and the features of the face became coarse, and the hands and feet became larger over a period of seven years. Her weight increased from 7½ st. to 10 st. 2 lb. Three years before admission she had first noticed some prominence of the eyes. Excessive thirst had been the symptom which led her doctor to diagnose diabetes mellitus. Menses had commenced at the age of 14 and were regular until the age of 23, since when there had been amenorrhœa. For three months

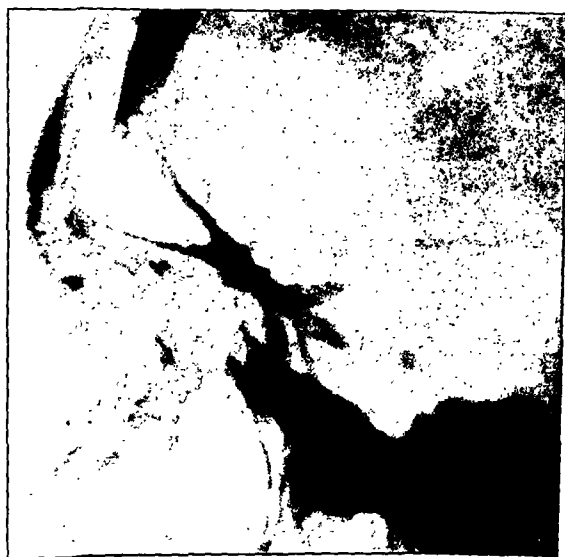


FIG. 6 (Case III, G. F.).—X-ray skull, showing enlargement of sella turcica.

she had had left frontal headache and misty vision and Mr. Goulden found she was developing diabetic cataracts. The ankles occasionally swelled and there was dyspnoea on exertion.

On examination, there were typical acromegalic stigmata—slight ridging of scalp, enlargement of nose, lips, chin and tongue, but normal incisor bite; moderate enlargement of hands and feet with spatulate fingers. The skin of the face was thick, greasy and rosaceous, and there was a marked moustache and beard. Moderate bilateral exophthalmos, slight thyroid enlargement. The pubic

29, 1947, when one needle containing 3.7 m.c. of radon was inserted into the pituitary gland. Her condition after the operation was satisfactory for about two weeks, there being no significant change in the ketosteroid excretion, renal functions, and glucose tolerance tests. Thereafter, she became increasingly drowsy, not taking nourishment, responding to directions but not speaking. On the nineteenth post-operative day the pupils reacted only sluggishly, the limbs were hypotonic but the reflexes were all normal. She was incontinent and was losing weight; there was no polyuria, sweating or pyrexia and the B.P. was 90/70. The lumbar cerebrospinal fluid was under normal pressure, contained no excess cells, but the protein was very high (200 mg. %). Dr. Simpson and I thought she was passing through a phase of acute pituitary cachexia, but the fasting blood sugar was 118 mg. on one day and on another was 222 mg. %, and a five-hour sugar tolerance curve showed no significant abnormality. She was given a high protein diet by nasal tube, adrenal cortical extract and testosterone with little apparent benefit. Occasionally she became more alert, but by the sixth week she had developed slight pyramidal signs on the right side, a waxy flexibility of the limbs, and equivocal bitemporal visual field defects. Dr. Russell Brain thought the condition one of radiation encephalopathy. A ventriculogram was carried out on January 1, 1948, demonstrating general ventricular dilatation (fig. 9.) This was compatible with diffuse cerebral atrophy from irradiation, but might have



(A) (B)  
FIG. 10 (Case V, B.S.).—Pituitary gland: cleft produced by radon "needle" surrounded by necrosis. (Stained H. and E. A  $\times 7$ ; B  $\times 52$ .)

been due to an obstructive hydrocephalus from posterior fossa adhesions, particularly as a previous lumbar encephalogram had been unsuccessful. In order to clarify this point, dye was introduced into the ventricles, followed by a lumbar puncture in order to recover the dye if there was free communication. No dye was present after one hour. Nine hours later she was unconscious and her breathing stertorous but she immediately improved after tapping the ventricle and allowing the escape of cerebrospinal fluid which was under increased pressure. For several hours she remained apparently in a satisfactory condition and then suddenly died, about half-an-hour after having had a drink. Post-mortem examination confirmed the symmetrical and generalized ventricular dilatation seen in the ventriculogram and no obstructive lesion could be demonstrated. The posterior part of corpus callosum showed some softening and cavitation. The walls of the lateral and third ventricles were stained by the methylene-blue introduced during the test, and which had given rise to an acute ependymitis with exudate and microscopic foci of haemorrhage. There was no histological evidence of radionecrosis in the brain, but there was considerable destruction of the pituitary tissue by the radon seed (fig. 10), and slight hyaline change in the remaining basophil cells, and slight hyperplasia of suprarenal cortex. For intraventricular injection, phenolsulphophthalein is usually employed and without ill-effect, but by a most unfortunate error in this case, methylene-blue was used and in an excessive dose; in small amounts it is unlikely to produce a severe reaction, but in this case it was undoubtedly responsible for an irritative ependymitis which hastened if it did not cause the fatality.

The approach to the sella turcica has been the same as that commonly employed for pituitary tumours, namely a frontal craniotomy and intradural elevation of the frontal lobe, exposing the diaphragma sellae between the optic nerves. In the cases of basophilism the operation has not been particularly difficult, although if the chiasm were found to be pre-fixed there might be too little room in which to manipulate the radon seeds into position. The precise relation between the anterior boundary of the sella and its diaphragm is important, for if the diaphragm lies much below the level of its anterior bony attachment, it is

hair on her face and shortly afterwards developed throbbing headaches accompanied by nausea which interfered with her duties in the A.T.S. where she served for four years. About two years later her weight gradually increased, reaching a maximum of 14 st. as against an earlier 8 st. Red streaks were noticed around the abdomen. In July 1946 she was given deep X-ray therapy (2,600 r) to the pituitary at a hospital in Palestine, without benefit. During March and April 1947 a further course of deep X-ray treatment (5,061 r) was given by Professor Windeyer at the Middlesex Hospital. After this,

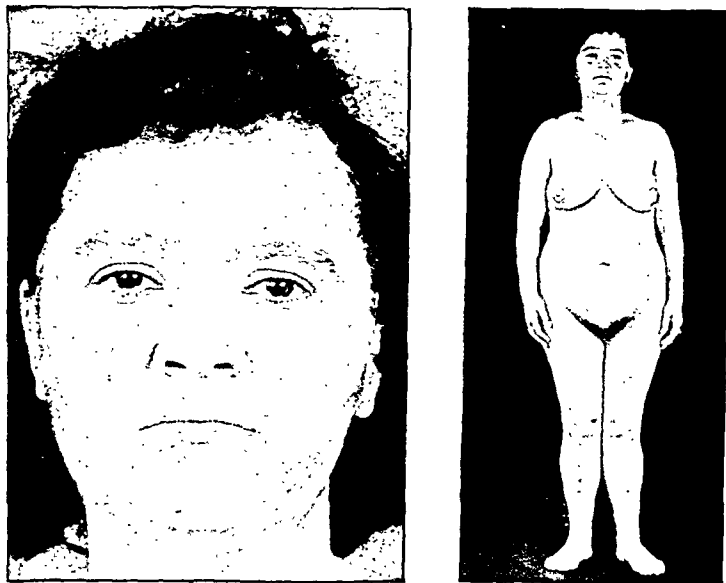


FIG. 8 (Case V, B. S.).—Pre-operative.

there was some temporary lessening of headaches, and her weight diminished to 10 st. 8 lb., though this might have been due to a 900 calorie diet during this period. There was no significant menstrual disturbance, some polydipsia, dyspnoea on exertion and anorexia. No significant points in family or personal history. *On examination* she was intelligent and alert, moderately obese, with a dusky-coloured skin and brown lineæ atrophicæ around abdomen. There was considerable hair on the face but not excessive elsewhere. The optic fundi and visual fields, the rest of the central nervous system and other systems were normal. The blood-pressure fluctuated between 130/90 and 95/60. Urine normal, fluid balance normal. 17-ketosteroids in February 1947, 10.5 mg. per twenty-four hours and, in October 1947, 16 mg. per twenty-four hours. A sugar tolerance curve gave a high peak (200 mg.%) at one hour. X-ray of the sella turcica showed no enlargement. Operation was carried out on October

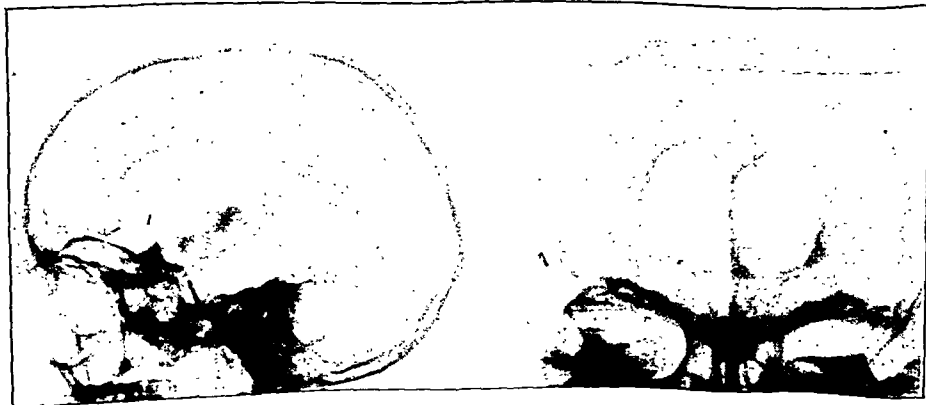


FIG. 9 (Case V, B. S.).—Generalized ventricular dilatation. Radon seed in sella turcica.



treatment has previously been given. It is now well recognized that radionecrosis of the brain can be readily produced if a maximum course of radiation is subsequently followed by a further course. This may hold true for other tissues including the pituitary gland, and may explain why 3.0 m.c. effected a cure in the first patient who had previously had deep X-ray therapy, but in the second patient, who had no X-radiation, 3.7 m.c. was only partly beneficial, and in the last patient, who had two courses of X-radiation, 3.7 m.c. produced marked cytological damage.

After my experience with the case of acromegaly in which a massive eosinophilic adenoma was present, I feel sceptical whether radon implantation is a useful procedure in a patient who has radiographic enlargement of the sella, indicating a frank intrasellar tumour. In this particular case, I had hoped rather naïvely to avoid the obvious surgical risks of evacuating the tumour, imagining that I should be able merely to implant the seeds. But I had not anticipated the tension within the tumour and its vascularity, which prevented such a simple manoeuvre, and compelled me to remove some of the tumour. In fact, operations on this type of tumour in which there are extrasellar extensions normally carry a very high mortality, and this patient would probably have died even if the usual surgical removal had been performed. A transphenoidal approach might be considered, although there would be the risk that the radon seeds might unwittingly be thrust through the capsule of the tumour within the cranium, causing intracranial hæmorrhage.

In the last case, death occurred about nine weeks after the operation, and was doubtless precipitated by the intraventricular methylene-blue causing ependymitis. But I am not satisfied that this was entirely responsible, and I doubt if such would have happened in a normal brain. The post-operative sequelæ were very unusual, and cannot be satisfactorily explained from one's experience in operations on brain tumours. Although histological evidence of radiation encephalopathy is lacking, there is unequivocal evidence of hydrocephalus compatible with atrophy of the brain by deep X-ray therapy. We have no ventriculographic evidence of the size of the ventricles before the operation, but the ease with which the frontal lobe was elevated after evacuating the ventricle leads me to believe that the hydrocephalus was already present, and possibly the result of her previous irradiation. Another significant abnormality suggesting active brain damage was the high protein in the C.S.F., but no pre-operative sample was taken for comparison. The neurological signs which eventually developed were what one might have expected from a radiation encephalopathy affecting particularly the frontal lobes. The mental retardation, paucity of voluntary movement, incontinence, anorexia and wasting produced a picture very like that seen in prefrontal leucotomy, when the division of the frontal lobe white matter has been made in a plane too posterior, and which usually ends fatally. On the other hand, part of the early post-operative state may have been due to pituitary cachexia, and it is difficult to apportion responsibility. From this case one can learn that where a full course of deep X-ray treatment has been given, caution must temper one's decision to implant radon. I should certainly advise a preliminary ventriculography in order to determine whether or not there was significant atrophy of the brain, and in doubtful cases it might be wise to allow a year to elapse before using radon. Not only would this allow more time for radiation effects to subside and also for any ventricular enlargement to become manifest, but it would demonstrate more clearly the necessity for further treatment.

## Radiotherapy in the Treatment of Pituitary Basophilism and Eosinophilism

By FRANK ELLIS, M.D.

THE aim of any patient in seeking treatment is to be able to rid himself of some organic or functional process which prevents him from leading a normal, carefree life. The best medical practice is to rid the patient of the basic pathological cause and to correct the secondary processes to which it may have given rise. In treating these pituitary conditions both these desiderata are difficult to carry out, but there is little doubt that, in the case of pituitary basophilism, to correct the essential underlying cause will result also in the automatic disappearance of most of the secondary changes which are so mentally and physically distressing to the patient and in the case of eosinophilism, while the patient may retain stigmata of the disease, a symptom-free existence may be possible except for the mental distress which acromegalic features cause, particularly to women. A partial relief of

difficult to see it, to incise it in the right place, and to coax the seed home. A special carrier for the seed might be devised, but I have failed to find a suitable shape for it, as there is no room to allow of any bulky instrument. The length of the seed is of some importance, those I have used have all been 1 cm. long, the platinum screen being 0.5 mm. thick. A shorter needle would be more difficult to handle, and a longer one would be too big to manipulate in the confined space available and might not be contained by the sella: in the last case, 2 mm. of the needle remained above the diaphragm (fig. 11). I think two seeds are better than a single one, as one can place them so as to get a more widespread effect; if out of alignment there will be less error than if a single seed is inserted in bad position. I do

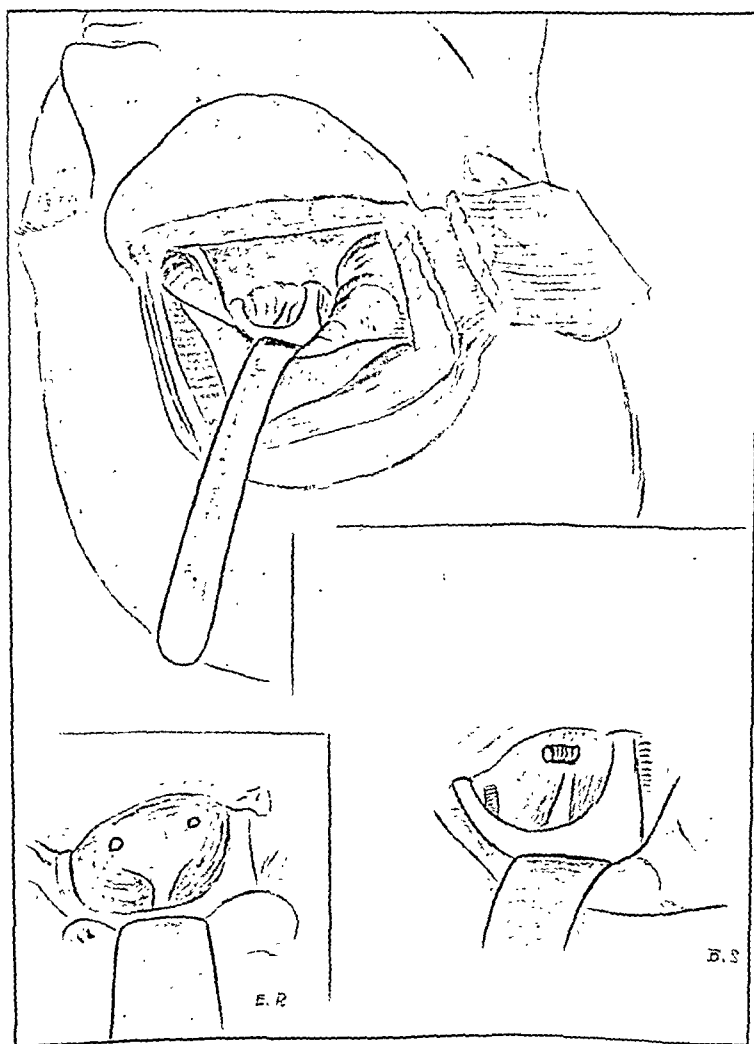


FIG. 11.—Operation for implanting radon.

not think that we can yet be certain of the correct dose of radon. In the fourth case (D. L.), in which there has been virtually no change, only 1.1 m.c. was inserted; this small dose was supplied in error, only appreciated afterwards, and I think can fairly be held responsible for the failure. In the best case (M. F.), the first, 3.0 m.c. was used; in the next case (E. R.), with moderate improvement, the dose was 3.7 m.c., and the same dose was used in the last, the fatal case—in which histologically the gland was considerably damaged. When deciding the dose I think it important that attention should be paid to whether or not deep X-ray

treatment has previously been given. It is now well recognized that radionecrosis of the brain can be readily produced if a maximum course of radiation is subsequently followed by a further course. This may hold true for other tissues including the pituitary gland, and may explain why 3.0 m.c. effected a cure in the first patient who had previously had deep X-ray therapy, but in the second patient, who had no X-radiation, 3.7 m.c. was only partly beneficial, and in the last patient, who had two courses of X-radiation, 3.7 m.c. produced marked cytological damage.

After my experience with the case of acromegaly in which a massive eosinophilic adenoma was present, I feel sceptical whether radon implantation is a useful procedure in a patient who has radiographic enlargement of the sella, indicating a frank intrasellar tumour. In this particular case, I had hoped rather naïvely to avoid the obvious surgical risks of evacuating the tumour, imagining that I should be able merely to implant the seeds. But I had not anticipated the tension within the tumour and its vascularity, which prevented such a simple manoeuvre, and compelled me to remove some of the tumour. In fact, operations on this type of tumour in which there are extrasellar extensions normally carry a very high mortality, and this patient would probably have died even if the usual surgical removal had been performed. A transphenoidal approach might be considered, although there would be the risk that the radon seeds might unwittingly be thrust through the capsule of the tumour within the cranium, causing intracranial hæmorrhage.

In the last case, death occurred about nine weeks after the operation, and was doubtless precipitated by the intraventricular methylene-blue causing ependymitis. But I am not satisfied that this was entirely responsible, and I doubt if such would have happened in a normal brain. The post-operative sequelæ were very unusual, and cannot be satisfactorily explained from one's experience in operations on brain tumours. Although histological evidence of radiation encephalopathy is lacking, there is unequivocal evidence of hydrocephalus compatible with atrophy of the brain by deep X-ray therapy. We have no ventriculographic evidence of the size of the ventricles before the operation, but the ease with which the frontal lobe was elevated after evacuating the ventricle leads me to believe that the hydrocephalus was already present, and possibly the result of her previous irradiation. Another significant abnormality suggesting active brain damage was the high protein in the C.S.F., but no pre-operative sample was taken for comparison. The neurological signs which eventually developed were what one might have expected from a radiation encephalopathy affecting particularly the frontal lobes. The mental retardation, paucity of voluntary movement, incontinence, anorexia and wasting produced a picture very like that seen in prefrontal leucotomy, when the division of the frontal lobe white matter has been made in a plane too posterior, and which usually ends fatally. On the other hand, part of the early post-operative state may have been due to pituitary cachexia, and it is difficult to apportion responsibility. From this case one can learn that where a full course of deep X-ray treatment has been given, caution must temper one's decision to implant radon. I should certainly advise a preliminary ventriculography in order to determine whether or not there was significant atrophy of the brain, and in doubtful cases it might be wise to allow a year to elapse before using radon. Not only would this allow more time for radiation effects to subside and also for any ventricular enlargement to become manifest, but it would demonstrate more clearly the necessity for further treatment.

## Radiotherapy in the Treatment of Pituitary Basophilism and Eosinophilism

By FRANK ELLIS, M.D.

THE aim of any patient in seeking treatment is to be able to rid himself of some organic or functional process which prevents him from leading a normal, carefree life. The best medical practice is to rid the patient of the basic pathological cause and to correct the secondary processes to which it may have given rise. In treating these pituitary conditions both these desiderata are difficult to carry out, but there is little doubt that, in the case of pituitary basophilism, to correct the essential underlying cause will result also in the automatic disappearance of most of the secondary changes which are so mentally and physically distressing to the patient and in the case of eosinophilism, while the patient may retain stigmata of the disease, a symptom-free existence may be possible except for the mental distress which acromegalic features cause, particularly to women. A partial relief of

symptoms is by no means as satisfactory as complete relief and it is desirable not to introduce into the picture a new set of symptoms due to complications caused by the treatment.

In assessing methods of treatment, moreover, it is essential to be sure of the condition to which the treatment has been applied, and in considering radiation therapy it is important to realize that variations in technique and the infinite possible variety of the dose and time relations may have effects both on normal and pathological tissues, and that definite effects on normally functioning endocrine tissue have not hitherto been demonstrated except in the case of the ovary where the effect is secondary to the destruction of dividing cells.

*Pituitary basophilism.*—The syndrome of pituitary basophilism was first described by Harvey Cushing in 1932 (*Bull. Johns Hopk. Hosp.*, 50, 137). The cardinal symptoms and signs are obesity, acrocyanosis, loss of sexual activity, hirsutism, cutaneous striation and pigmentation, polycythæmia, hypertension, skeletal decalcification and hyperglycæmia. Secondly the patients experience emotional upset, changes due to the mechanical strain imposed on the cardiovascular system, effects of calcium stones in the kidneys and changes in the mechanical efficiency of the skeleton. That this syndrome is due entirely to basophil tumours of the pituitary as Cushing originally postulated is now untenable since cortical adrenal tumours and thymic tumours have been shown by Crooke in 1935 to be associated with the syndrome while in some patients with definite basophil adenomas the syndrome was only partially present in cases reported by Russell, Evans and Crooke in 1934 (*Lancet* (ii), 240). Crooke, however, considered that in the basophil cells of the pituitary (as distinct from those of the basophil tumour when it was present) there was, in all cases of Cushing's syndrome, a hyaline, highly refractive cytoplasmic content which stained characteristically and was not present even when there was a basophil tumour if this was not associated with Cushing's syndrome; and did not occur in the cells of the tumour even if Cushing's syndrome was present. Moreover, Lescher (1935, *Quart. J. Med.*, 4, 23) reported a small non-encapsulated collection of basophil cells 0.3 mm. in diameter in the pituitary, in a case of adrenocortical carcinoma, with additional associated general increase in basophil and acidophil cells of the gland, in a case of Cushing's syndrome. We have, therefore, as a basis for the condition a change in the basophil endocrine cells of the pituitary whether or not there is actually a tumour in the pituitary. The result appears to be a polyglandular disturbance.

From the point of view of treatment it would appear to be necessary to deal with the underlying primary pathological disturbance, whether in the adrenal, the thymus or the pituitary. In this discussion we are concerned with the pituitary, and so the importance of growths in the other two situations is that they should be excluded before treating the pituitary or drawing any conclusions from the effect, or absence of effect, of such treatment. A thymic tumour which is not visible radiologically can only be excluded by a major thoracic operation which is unjustifiable. An adrenal tumour may be looked for by clinical examination, X-rays of the kidney region with or without pyelography and perirenal air insufflation and by investigation of the 17-ketosteroids excretion in the urine. In 5 cases of the 8 with which I have had to deal, such estimations were carried out and in only 1 did they indicate an abnormally high excretion. It was not constantly high and the proportion of the beta form was only 5%. The value fell from 42 to 27 and 15.7 after removal of one adrenal gland, not found to contain a tumour, and then rose again to 35.8 in two months. One year later the value was 18. Pattison, A. R. D., and Swan, W. G. A. (*Lancet* (i), 1265, 1938), considered adrenal exploration essential before the drastic step of exploring and needing the pituitary gland. This seems desirable and almost essential. When a pituitary tumour exists it is usually very small and causes no appreciable enlargement of the pituitary fossa.

*The effects in the untreated condition.*—Before deciding on the treatment of any medical condition one should have in mind a clear idea of the relative dangers of the condition and the treatment. There seems little doubt that some cases tend to improve spontaneously. Two young men referred to me have both improved without treatment. One woman of 51 who came from a psychiatrist with all the cardinal symptoms and signs except osteoporosis, which started eighteen years ago, has been improving during the last three years, having refused any treatment. It is interesting that she had the ovaries removed for metrorrhagia seven years ago. The pituitary condition might have been responsible for the metrorrhagia. She was not a very marked case. Because of this tendency to spontaneous recovery, treatment should not be precipitate but due regard must be had for the profound effect on the life of a young woman of this distressing condition. In the very severe cases the adiposity, hirsuties and psychological changes apart from the danger to life of the cardiovascular and skeletal changes may make any risk seem justifiable. As a clinical point the colour of the atrophic striæ is useful. If they lose their characteristic purple colour it is said to indicate improvement. In such a case treatment should probably be withheld for a time at any rate. Cushing reports an untreated case, well after twenty years.

*The effects of X-ray treatment* have never, in my experience, been dramatic. In published cases reviewed by Freyberg, Barker, Newburgh and Collier (1936) 12 of 28 cases treated showed improvement and 16 no improvement. Those showing most improvement had received large doses of radiation. Luft (1946) reported cure in 4 cases of 7. The other 3 cases relapsed after initial improvement. Eisenhardt and Thompson note only one case improved out of 18 treated (see Table I).

*Treatment by radon insertion* has obvious surgical dangers. These, however, may be overcome with experience and technique. Mr. Northfield has reported some encouraging results and 2 cases treated by the late A. R. D. Pattison, neurosurgeon to the Newcastle General Hospital, were reported in 1938 (*Lancet* (i), 1265). The doses which were used in the pituitary fossa were in one case 4 m.c. and in the others 9 m.c. This implies a minimum dose in the pituitary fossa of about 17,000 r in one case and 38,000 r in the other with corresponding maximum doses of about 340,000 r and 750,000 r. Both cases had already had deep X-ray without success. In ordering radon for Mr. Northfield's cases I aimed at a minimum of 6,000 r and felt very apprehensive of the possible effects of this dose in causing pituitary extirpation, a condition I have always regarded as serious. Dr. Thurgar informs me that of the 2 cases reported in 1938 which initially improved so dramatically, the first died in 1942 of meningitis and the second died subsequently in a mental home.

*Clinical results of treatment by X-rays.*—In only one case treated by me was the improvement really satisfactory. In some cases headache has been improved. The symptom which is most recalcitrant is the adiposity. One patient considered as slightly improved is very fat (13 st. as compared with 15 st. before treatment), but was considered by Dr. Crooke to have no active basophilism. A patient treated in 1943 wrote three months ago to say that the hirsuties is improving now. She is the girl who had a normal adrenal gland removed in 1946. No patients have had visual symptoms before or after treatment except one case treated previously in Jerusalem and for whom I do not know the dose and technique used. The small size of the tumour in such cases makes it unlikely that such symptoms are due to it as in other pituitary tumours. One case of unilateral blindness has been reported to me one year following a dose of 5,500 r in three weeks, and another case following a dose of 2,440 r in three weeks. While in the first case the treatment might possibly be partly responsible it seems to me in the second case highly unlikely, and some other cause must be sought. The proximity of the visual apparatus obviously imposes an extra need for care. The two London Hospital cases who did not respond to treatment were treated by Mr. Northfield by insertion of a radon seed, but both died shortly after.

*Relationship of dose to result* (see Table II).—Apart from possible damage the question arises as to whether there is any specific dose of radiation which might be expected to give a favourable result. Cases showing improvement in the above collected series have received doses at the pituitary of 2,000–3,000 r in three weeks, 4,500 r in four weeks and 6,000 r in five weeks. My view is that 4,500 r in four weeks at the pituitary is the optimal dose. If this does not produce an effect no further deep X-ray treatment should be given. The need for high dosage and the need for planning the treatment mean that the dose to be given must be prearranged and, while it might be diminished if unexpected complications develop during treatment, it should not be diminished for favourable results.

*Duration of result.*—All the cases treated in my series have been observed for more than three years, and have tended to improve further, rather than regress. The improvement from Newcastle was reported by Dr. Thurgar as temporary. One young man from the Christie Hospital, Manchester, is well after eight years.

*Pituitary eosinophilism* as a cause of acromegaly, or, less commonly, of gigantism, is a clinical entity needing no elaboration. The chief features as shown by my series of cases are excessive growth causing acromegalic features or gigantism, headache, visual disturbances and other endocrine disturbances such as diabetes mellitus, loss of libido in males, amenorrhœa and, in one case, thyroid disturbance. Also they seem to be prone to develop a hypertrophic type of osteoarthritis affecting especially the hips and knees.

The underlying pathological entity is generally considered to be an eosinophil adenoma or eosinophil cells in a chromophobe adenoma. Many of the tumours while smaller on the average than the chromophobe adenomas are so large as to cause enlargement of the pituitary fossa. From the point of view of assessing the value of treatment it is important to know whether spontaneous cessation of activity can occur and whether acromegalic changes can occur as a result of physiological hypertrophy of the eosinophil tissue in the gland, especially in cases where there is no enlargement of the fossa or pressure on the optic chiasma. Whether such "physiological" cases of spontaneous cessation of activity do occur I do not know, but such cases must be very much in the minority.

Without treatment continued aggravation of all the symptoms occurs, the patients being constantly affected by headache, in danger of increasing blindness, of further emphasis of their local or general overgrowth and of other changes due to pressure atrophy of the rest of the pituitary. Moreover, they are weak and have no zest for life, living continually at a low level of vitality. The outcome is likely to be fatal. All 4 patients in my series who died had hæmorrhage, 3 into the tumour and 1 into the adjacent brain. Treatment therefore is indicated and the taking of risks is justifiable.

The results of X-ray treatment reported in the literature indicate an encouraging response to radiation. The earliest reports were in 1909 when Gramegna reported the successful treatment of a case of acromegaly and Bécère reported on a case of gigantism in a girl of 16. Both cases showed long-continued improvement. In 1925 Dott, Bailey and Cushing advocated the use of radiotherapy in selected cases. Table III shows some published results. In Vaughan's cases those he reports as good result are put in the slight improvement column, excellent results as marked improvement, and poor results as no change. The case reported by Weinstein is of interest because the woman menstruated at 36 years

TABLE I.—PITUITARY BASOPHILISM

| Author                      | No. | Improved |        | Worse | No change |
|-----------------------------|-----|----------|--------|-------|-----------|
|                             |     | Slight   | Marked |       |           |
| Freyberg <i>et al.</i> ..   | 28  |          | 12     |       | 16        |
| Luft ..                     | 7   | 3        | 4      |       |           |
| Eisenhardt <i>et al.</i> .. | 18  |          | 1      |       | 17        |
| Cushing ..                  | 2   |          | 2      |       |           |
| Ellman and Vilvandré ..     | 1   |          | 1      |       |           |
| Tchaperoff (2,200 r) ..     | 4   |          | 4      |       |           |
|                             | 60  |          | 27     |       |           |

TABLE II.—PITUITARY BASOPHILISM

| Hospital                    | No. | Improved                         |         | Worse   | No change           |
|-----------------------------|-----|----------------------------------|---------|---------|---------------------|
|                             |     | Slight                           | Marked  |         |                     |
| London Hospital             |     |                                  |         |         |                     |
| Treated .. ..               | 5   | 2 ( $\frac{1.2}{3.0}$ )          | 1 (4.5) |         | 2 ( $\frac{5}{4}$ ) |
| Untreated .. ..             | 3   |                                  | 3       |         |                     |
| Other Hospitals A (2.5-3.0) | 7   | 4                                |         |         | 3                   |
| B .. ..                     | 4   | 2 ( $\frac{2.0}{6.0}$ )          | 1 (2.0) | 1 (5.5) |                     |
| C .. ..                     | 1   |                                  | 1 (1.3) |         |                     |
| D .. ..                     | 2   | 2 ( $\frac{3.0}{2.0 \times 2}$ ) |         |         |                     |
| E (2.0-3.0)                 | 3   | 2                                | 0       | 0       | 1                   |
| Treated cases .. ..         | 22  | 12                               | 3       | 1       | 6                   |

Figures in brackets indicate dosage levels in thousand roentgens.

TABLE III.—EOSINOPHIL ADENOMA

|                        | No. | Worse    | No change | Improved |           |
|------------------------|-----|----------|-----------|----------|-----------|
|                        |     |          |           | Slight   | Marked    |
| Dyke and Hart, 1936 .. | 25  | 6        | 9         | 8        | 2         |
| Vaughan, 1938 ..       | 34  |          |           |          |           |
| Surgery + DX ..        | 12  | 6 (Died) | —         | 5        | 1         |
| DX only ..             | 22  | 7 (Died) | 5         | 8        | 2         |
| Weinstein, 1939 ..     | 1*  |          |           |          | 1         |
|                        |     |          |           |          | (7 years) |
| Total                  | 60  | 19       | 14        | 21       | 6         |
|                        |     |          |           | 45%      |           |
| Radiotherapy only ..   | 48  | 13       | 14        | 16       | 5         |
|                        |     |          |           | 44%      |           |

\*This patient had normal baby after five years.

of age after four years' amenorrhœa, three years after starting deep X-ray treatment. She had a miscarriage at 37 years and a normal baby was born when she was 39 years.

Table IV gives an assessment of the results of radiotherapy in my series and from some other centres. The clinical assessment is unlikely to be uniform between the degrees of improvement but is reasonably accurate for the other columns.

The salient feature is that for doses to the pituitary less than 3,000 r about two-thirds of the cases improve. The high doses seem to produce worse results. The cases treated in the London Hospital were given for the most part 1,200–1,800 r in about three weeks since 1944. Previous to this several cases were sent for treatment which had already been treated over a period of years, at much lower dosage rates but to doses of 3,000–4,000 r. 2 cases with severe progressive diabetes mellitus were given larger doses (4,000 r on top of an initial 1,200 r) and both died with hæmorrhage, one of them following operation, and the other fourteen months after her last treatment. The latter was diagnosed histologically as acromegalic carcinoma. One patient was started on a further course of treatment because of defective visual fields, which proved to have been taken by an unreliable observer. Whether his second course of treatment has done harm remains to be ascertained, as only three

TABLE IV.—EOSINOPHIL ADENOMA

| Hospital                  | No.   | Died | Worse | No change | Improved Slight | Improved Marked |
|---------------------------|-------|------|-------|-----------|-----------------|-----------------|
| London Hospital           |       |      |       |           |                 |                 |
| All cases (1,200–1,500 r) | 24    | 5    | 0     | 1         | 7               | 11              |
| After surgery             | .. 2  | 1    | 0     | 0         | 0               | 1               |
| Before surgery            | .. 1  | 1    | 0     | 0         | 0               | 0               |
| Radiation only            | .. 21 | 3    | 0     | 1         | 7               | 10              |
| Other hospitals:—         |       |      |       |           |                 |                 |
| A .. 5                    |       | 0    | 0     | 2         | 1               | 2               |
| B .. 11                   |       | 7    | 2     | 0         | 0               | 2               |
| C .. 2 (Post. op.)        |       | 0    | 0     | 1 (3.0)   | 0               | 1 (3.0)         |
| D .. 8                    |       | 0    | 0     | 4 (4.2)   | 3               | 1               |
| E .. 2                    |       | 0    | 0     | 0         | 2               | 0               |
| (2.0–3.0)                 |       |      |       |           |                 |                 |
| Radiation only            | .. 47 | 10   | 2     | 7         | 13              | 15              |
|                           |       |      |       |           |                 | 59%             |

TABLE V.—SYMPTOMS: RESPONSE TO TREATMENT

24 Cases of Eosinophil Adenoma

|                             | No. | Improved |
|-----------------------------|-----|----------|
| Headache .. ..              | 19  | 11       |
| Loss of libido .. ..        | 9   | 4        |
| Menstrual .. ..             | 4   | 2        |
| Weakness .. ..              | 5   | 3        |
| Vertigo .. ..               | 3   | 2        |
| Visual .. ..                | 5   | 4        |
| Diabetes mellitus .. ..     | 4   | 0        |
| Enlarged pituitary fossa .. | 19  |          |
| Normal pituitary fossa ..   | 5   |          |

TABLE VI.—AGE INCIDENCE

|                | 10–19 | 20–29 | 30–39 | 40–49 | 50–59 | 60–69 |
|----------------|-------|-------|-------|-------|-------|-------|
| Basophilism    |       |       |       |       |       |       |
| Female 8 .. .. | 0     | 2     | 4     | 1     | 1     | 0     |
| Male 5 .. ..   | 1     | 4     | 0     | 0     | 0     | 0     |
| Eosinophilism  |       |       |       |       |       |       |
| Male 18 .. ..  | 1     | 5     | 6     | 3     | 2     | 1     |
| Female 6 .. .. | 0     | 3     | 2     | 1     | 0     | 0     |

months have elapsed. Another patient who had 3 courses of treatment had his first epileptiform fit ten months after the last course of treatment. I consider that this might be due to the radiation causing necrosis and glial reaction in the radiated normal brain, even though the doses were not very large. Eight months or more is I think the time at which such reactions can occur.

An assessment of the improvement of various symptoms is made in Table V for cases where the symptoms are stated in the notes. The headache present after operation does not seem to improve. Visual symptoms seem to improve in a high proportion of cases. In no case was diabetes mellitus influenced and I feel that in 2 cases at least treatment may have been pushed unduly to try to get rid of intractable diabetes, to the ultimate disadvantage of the patients. On the other hand the fact that these two patients were both requiring heavier insulin dosage, up to 200 units daily, indicated that some further active treatment was required. The question is whether radiation treatment should be given beyond a certain limit. One of these cases of diabetes mellitus was said to be a carcinoma but purely because of local invasion. Recurrence of headaches may, I think, follow a second course of radiation. I have never seen worsening of the visual fields follow the commencement of a course of radiation. The recovery of sexual function seems to require a relatively long time—up to three years.

*The age incidence* of the cases is seen in Table VI. The basophilism series includes cases from other hospitals. The eosinophilism series consists of London Hospital cases only. It is seen that the incidence of basophilism in males is in young adults, and in females appears to occur at a later age. Eosinophilism shows a higher male incidence in the ratio 3 : 1 and the highest age incidence between 20 and 40.

*Radiotherapy technique.*—I propose to mention a few principles which seem to me of importance in connexion with the technical side, apart from dosage and repetition of treatment.

(1) The minimum voltage used should be 180–200 kV. with 0.5–1 mm. copper filter and not less than 40 cm. F.S.D. so as to get the necessary depth dose to the pituitary.

(2) The fields used should, I think, be kept to 4 or 5 cm. for eosinophil tumours and 3–4 cm. for basophil tumours. This means accurate localization and direction because of the greater danger of missing the pituitary fossa with a small field. The advantage of small fields is that damage to normal brain tissue is minimized. This is particularly important in basophil tumours where a high focal dose is required. To use a field 3 in. across to hit a cavity  $\frac{1}{2}$  in. across seems extravagant.

(3) For acromegaly I think fields should be directed downwards from the front. The filtration of the bone in the base of the skull is serious for lateral and true anterior fields. Only 3 or 4 fields are needed.

(4) For basophilism many fields should be used so as to minimize the risk of permanent bald patches. Eight fields accurately directed can all be about the same distance from the pituitary fossa if the anterior half of the cranium is used.

*X-rays versus radon.*—A most important general principle in radiotherapy is to minimize the amount of radiation of normal tissue; radon in the pituitary fossa is, from this point of view, very good technique. The approach should be as by Pattison and Northfield, so that the seed or seeds can be accurately placed in the anterior half and not, as suggested by Lodge, by the orbito-nasal route.

The dose must be found by experience but a minimum dose of 4,000 r to the pituitary anterior lobe should be adequate and it is better to use a relatively small dose rather than risk the over-irradiation causing the death of the patient, as I think it might have done in Pattison's cases. I should recommend two 0.5 m.c. seeds 1 cm. apart in the anterior half of the pituitary fossa. A relatively slow result should be aimed at in basophilism; a quick effect may indicate over-irradiation.

If X-ray therapy fails in acromegaly I think that, rather than tumour removal, the use of radon implantation as the next step may be less dangerous and more effective since removal is probably never complete. It should be possible to implant such a tumour so as to give a uniform dosage, if the Paterson-Parker rules governing spacing of radiation sources to give a homogeneous dose can be observed. A minimum dose of 3,000 r should be adequate.

Close co-operation between the radiotherapist and his neurological colleagues is essential.

I should like to acknowledge the co-operation of Mr. D. W. C. Northfield, Dr. Russell Brain, and Dr. A. C. Crooke. My thanks are also due to Dr. B. A. Stoll and Dr. F. Stansfield of my department for help in connexion with this paper.



The following is an extract from an account of his disease by a patient of mine:

As a youngster I am sure I rather enjoyed having my photograph taken. I don't think I was particularly conceited, but I always knew there was a pretty good chance I should "come out" rather well. Although my general physical development was fairly good, my small hands and rather thin neck were a family joke. The last time a photograph was taken of me in which I recognized myself instantly was towards the end of 1939. At this time I was about 5 ft. 11 in. tall, 38 in. chest, 32 in. waist and I weighed 13½ st.

During the last three months of 1941 and the first three of 1942 when I was aged 25 yrs., though I usually felt very well, I had occasional very severe headaches—usually in the morning, and wearing off during the day. I was also rather puzzled to find that my resting pulse-rate was persistently between 90 and 100 per min. In about February 1942 I had a "studio" photograph taken for my parents. It shows smooth rounded forehead, plump unlined cheeks, small nose and lips and chin. Eyes rather deep set and maxillary area small. Nevertheless I did not think it looked much like me nor did my mother and father. I believe the camera had recorded a change in my features not otherwise noticed.

After this I remember no particular related event for about a year. In September and October 1941 I was a maternity student and wearing size 7 or 7½ gloves.

From January to March 1942 I frequently experienced an uncomfortable fullness in the head as though my skull were stuffed with cotton-wool. Also a sensation of congestion in the neck. Both appeared to be brought on particularly by lying too flat in bed or by wearing too tight collars. At the beginning of the year I was wearing size 15½ collars and these rapidly became too small and I had to get all new shirts. At the same time I had a light, black pair of shoes which I wore infrequently. They had always been a close fit. I looked them out to wear for some occasion and found to my surprise I was quite unable to get them on.

I believe a considerable change in my facial appearance must have occurred between March 1942 and August of that year. Those whom I met daily appeared to notice little save that I looked ill.

From January to November 1943 I was studying for Finals and often felt very ill indeed. At other times, however, I felt quite moderately well. I could not sleep without 4 pillows. My head felt full and woolly much of the day and I would frequently wake in the morning and go to bed at night with a splitting throbbing left frontal headache. I put it all down to swotting, smoking and "sinus trouble". I used large quantities of ephedrine-in-oil nasal drops, and seemed to get a degree of symptomatic relief from them. I did not notice that my hands had increased in size, but they often felt swollen and the skin of my fingers felt thickened and stiff. Sometimes there was slight itching. Rather as if I'd been playing fives with no gloves. At other times this trouble would disappear, and my fingers then felt thin and supple. Also I often felt a bit dizzy when walking about and I often had unpleasant hot and cold flushes of the skin. I noticed that the hair on my chest and abdomen was becoming darker and coarser.

At breakfast one morning I found I couldn't read the newspaper with my left eye. I asked permission to see Mr. Summers. He told me I had acromegaly.

It may appear that I was rather dull not to have made the diagnosis myself at a much earlier stage. The idea did occur to me once or twice but seemed too ridiculous to be considered seriously. I was never really aware of any change in my features or my hands or feet. I only noticed that I could not wear old shoes or gloves and that photographs produced a series of what I considered to be poor pictures of me. In the high-pressure days and badly ventilated hospitals of 1943-44 everyone felt a bit out-of-sorts occasionally and headaches were not uncommon.

Mr. Summers placed me in the care of Dr. Ellis, Mr. Northfield and Dr. Russell Brain. I underwent a course of deep X-ray therapy. Within a few weeks my sight had recovered completely and the severe headaches ceased. Following the treatment I felt rather weak for about a month, and experienced a certain amount of nausea from time to time. My weight dropped down to 12 st.)

For the last four and a half years there has been so gradual but progressive improvement in my condition, it can only be appreciated by looking back.

The first year following the treatment I spent at sea with the M.N. and felt well enough to derive much pleasure from the rest and change. The hot and cold "flushes" which I had previously experienced returned. They appeared off and on for about eighteen months. I was told that my features rapidly regained some of their old expressiveness, and after this there appeared to be a very gradual ill-defined improvement in my appearance over two or three years. As far as I can gather, where once I looked ill and "a bit peculiar", I now look well and normal, if somewhat rugged. That is to say, comparison of photographs shows an obvious development of prominent brows, increased maxillary area, larger nose, thickened lips and slightly more prominent eyes.

During the first six months following the treatment I ceased snoring at night. I continued to experience discomfort on sleeping with a low pillow for about three years, and often had a sort of woolly headache in the mornings, but severe pains ceased to occur.

Until a year ago, my hands would often become "puffy" as previously described, and I often looked rather haggard in the mornings. I do not remember this happening in the last year. I have repeatedly

noticed, during the last four and a half years, a sensation of pressure between the eyes at times of strain or excitement (as for example, when I sat for an examination last year).

I am now very well indeed. Although leading a fairly sedentary life, my muscular development is considerable. I weigh 15½ to 16 st., 46 in. chest, 38 in. waist, 17 in. collar, size 8 gloves, size 10 shoes. I have recently shown that I can give a good account of myself in a heavy day's work on the farm. In fact my only remaining disability—if disability it is—was summed up by one of my patients who remarked "You look more like a prize-fighter than a doctor".

**Dr. A. C. Crooke:** Most of Cushing's original patients with basophilism got worse fairly rapidly and died, but many of the patients one sees now have a more chronic disease which fluctuates in severity for many years so that calculation of the effectiveness of a therapeutic agent is difficult. Mr. Frank Ellis's figures would be much more convincing if he could differentiate between those patients who were likely to die in a relatively short time and those who were not. In the former I doubt if X-ray therapy is effective, but radon implantation can produce a dramatic response, as Mr. Northfield has shown in his first case. This is borne out forcibly by the anatomical changes produced. I have examined pituitary glands from a number of patients of Sir Hugh Cairns who have had intensive radiotherapy for tumours in the region of the sella turcica but I have never seen any histological change in the pituitary glands which could be attributed to this treatment. Radon implantation on the other hand produces a large area of necrosis in the anterior lobe which is very striking on histological examination.

The answer to the question as to whether one radon seed or two should be used must be guided by the anatomy. Practically the whole blood supply to the human pituitary gland comes down the pituitary stalk in the pars tuberalis and enters the superior surface of the anterior lobe adjacent to the stalk. Here it divides into two groups of vessels which penetrate the substance of the anterior lobe and run downwards in connective tissue hila which can be recognized lying deep on either side of the mid-line. Two radon seeds might penetrate each of these hila and cut off the blood supply to most of the gland, but one seed inserted at the anterior edge of the superior surface and directed postero-inferiorly should miss them. I think, therefore, that one seed is likely to produce more uniform results.

**Dr. A. W. Spence, Dr. G. I. M. Swyer, Dr. C. N. Armstrong, Dr. Raymond Greene, Dr. R. D. Lawrence and Mr. J. Jackson Richmond** also took part in the discussion.

# PROCEEDINGS *of the* ROYAL SOCIETY OF MEDICINE

ISSUED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE

HONORARY EDITORS

ERIC A. CROOK      E. R. CULLINAN

EDITOR

J. M. BROWNE KUTSCHBACH

|                                           |                                 |
|-------------------------------------------|---------------------------------|
| G. S. W. ORGANE (Anæsthetics)             | F. T. RIDLEY (Ophthalmology)    |
| J. S. RICHARDSON (Clinical)               | H. L.-C. WOOD (Orthopædics)     |
| J. B. BROOKSBY (Comparative Medicine)     | C. S. HALLPIKE (Otology)        |
| E. W. PROSSER THOMAS (Dermatology)        | A. G. SIGNY (Pædiatrics)        |
| E. F. SCOWEN (Endocrinology)              | F. R. SELBIE (Pathology)        |
| ALLAN McFARLAN (Epidem. & State Med.)     | M. B. RAY (Physical Medicine)   |
| A. C. WHITE (Exper. Med. & Therap.)       | O. V. LLOYD-DAVIES (Proctology) |
| I. E. McCracken (History of Medicine)     | DENIS HILL (Psychiatry)         |
| W. A. MILL (Laryngology)                  | F. CAMPBELL GOLDING (Radiology) |
| MAURICE DAVIDSON (Medicine)               | CHARLES DONALD (Surgery)        |
| J. St. C. ELKINGTON (Neurology)           | G. M. FINDEAY (United Services) |
| LESLIE WILLIAMS (Obstetrics & Gynæcology) | A. CLIFFORD MORSON (Urology)    |
| B. W. FICKLING (Odontology)               |                                 |

SECRETARY OF THE ROYAL SOCIETY OF MEDICINE

G. R. EDWARDS



# MALE HORMONE

ROUSSEL

---

**TAB. METHYLTESTOSTERON. B.P.**

Glosso-Sterandryl—5, 10 and 25 mg.

**INJ. TESTOSTERON. PROP. B.P.**

Sterandryl—5, 10, 25, 50 and 100 mg.]

**IMPLANT** of 100 mg. TESTOSTERONE

Sterandryl—Implant.



ROUSSEL LABORATORIES LIMITED  
4, Golden Square, London, W.1

GERard 3111-2

# PROCEEDINGS OF THE ROYAL SOCIETY OF MEDICINE

Vol. XLII No. 11 November 1949

## CONTENTS

Whole  
Proceedings  
Page

### Clinical Section

*April 8, 1949*

- Cardiac Pain Due to Glucose Deficiency. ? Pituitary Dysfunction.—A. SCHOTT, M.D. 861  
 Tumour of Bile Papilla Treated by Transduodenal Excision.—FRANK FORTY, F.R.C.S. 862  
 Diaphragmatic Hernia Through the Right Foramen of Morgagni, Causing Asthma.—  
 LEO RAU, M.R.C.P. .. .. . 864  
 ? Strümpell-Marie Type of Spondylitis.—GERALD SLOT, M.D. .. .. . 865

*May 13, 1949*

- (1) Genito-Urinary Tuberculosis with Extensive Calcification of the Bladder .. .. . 866  
 (2) Calcification of Ascending Aorta as a Diagnostic Sign of Syphilitic Aortitis .. .. . 867  
 A. ELKELES, M.D.  
 Jejunal Insufficiency with Hypoproteinæmic Œdema.—E. MONTUSCHI, M.D., M.R.C.P. 868  
 Typhoid treated with Chloromycetin.—F. MURGATROYD, M.D., F.R.C.P., D.T.M. .. 869

### Section of the History of Medicine

- The Destruction of John Hunter's Papers.—DUNCAN C. L. FITZWILLIAMS, C.M.G.,  
 F.R.C.S. .. .. . 871

### Section of Neurology

*December 2, 1948*

- Somatic Movements of the Prematurely Born Fœtus—Film Demonstration.—IVY  
 MACKENZIE, M.A., B.Sc., M.D., F.R.F.P.S. .. .. . 877

*April 7, 1949*

- A Review of Cerebral Angiography.—JAMES W. D. BULL, M.D., M.R.C.P., D.M.R. . . 880

### Section of Psychiatry

- Clinical and Electroencephalographic Studies of Temporal Lobe Function.—J. H. REY,  
 M.D., D. A. POND, M.R.C.P., D.P.M., and C. C. EVANS, L.R.C.P., M.R.C.S. .. 891

### Section of Pædiatrics

*April 22, 1949*

- DISCUSSION: TOILET TRAINING IN EARLY CHILDHOOD. . . . . 905

*June 11, 1949*

- MEETING AT SOUTHMEAD HOSPITAL, BRISTOL  
 DEMONSTRATION OF NEONATAL DEPARTMENT, SOUTHMEAD HOSPITAL [Summary] .. .. 909  
 Obstetric-Pædiatric Relationships—Professor A. V. NEALE, M.D. .. .. . 910

MEETING AT THE CHILDREN'S HOSPITAL, BRISTOL

#### CASES

- I.—Œsophageal Hiatus Hernia with Ulceration of Lower Third of Œsophagus.—  
 A. V. NEALE, M.D., and R. H. R. BELSEY, M.S. . . . . 911  
 II.—Œsophageal Hiatus Hernia.—A. V. NEALE, M.D. .. .. . 912  
 III.—Œsophageal Hiatus Hernia.—A. V. NEALE, M.D., and R. H. R. BELSEY, M.S. .. 913  
 IV.—Congenital Hiatus Hernia.—BERYL CORNER, M.D., and R. H. R. BELSEY, M.S. .. 913  
 V.—Recurring Left Diaphragmatic Hernia with Intestinal Obstruction by Adhesions.—  
 R. V. COOKE, Ch.M., and BERYL CORNER, M.D. . . . . 914  
 VI.—Œsophageal Atresia and Tracheo-Œsophageal Fistula.—R. H. R. BELSEY, M.S. . . 915  
 VII.—Cæliac Disease in Twins.—BERYL CORNER, M.D. .. .. . 915  
 VIII.—Tuberculous Left Epididymis.—A. WILFRID ADAMS, M.S. .. .. . 916  
 IX.—Scurvy, with Bilateral Dislocation of the Lower Femoral Epiphyses.—A. V.  
 NEALE, M.D. .. .. . 916  
 X.—Calcifying Tuberculous Cold Abscess in Left Hypochondrium.—C. S. SHAW, M.B.  
 (for A. V. NEALE, M.D.) .. .. . 917  
 List of Demonstrations .. .. . 917  
 Congenital Anomalies of the Aortic Arch and Its Branches.—JOHN APLEY, M.D. .. 918

(Continued on next page)

## Section of Radiology

## COMBINED MEETING WITH THE BRITISH INSTITUTE OF RADIOLOGY AND THE FACULTY OF RADIOLOGISTS

|                                                                                                                                                                                         |     |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|
| DISCUSSION ON THE PHYSICAL, CYTOLOGICAL AND MEDICAL ASPECTS OF PROTECTION FROM IONIZING RADIATIONS WITH SPECIAL REFERENCE TO THE USE OF HIGH VOLTAGE X-RAYS AND RADIO-ISOTOPES. . . . . | 923 |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|

## Section of United Services

|                                                                       |     |
|-----------------------------------------------------------------------|-----|
| DISCUSSION: POST-GRADUATE MEDICAL EDUCATION IN THE SERVICES . . . . . | 935 |
|-----------------------------------------------------------------------|-----|

## Section of Dermatology

May 19, 1949

|                                                                                               |     |
|-----------------------------------------------------------------------------------------------|-----|
| Periarteritis Nodosa.—H. W. BARBER, F.R.C.P. . . . .                                          | 945 |
| For Diagnosis ? Dermatomyositis.—A. LYELL, M.B., and C. H. WHITTLE, M.D. . . . .              | 946 |
| (1) Balanitis Xerotica Obliterans . . . . .                                                   | 948 |
| (2) Kaposi's Hæmorrhagic Sarcoma. . . . .                                                     | 948 |
| P. D. SAMMAN, M.R.C.P. (for J. E. M. WIGLEY, F.R.C.P.) . . . . .                              |     |
| Lichen Planus.—G. B. MITCHELL-HEGGS, O.B.E., F.R.C.P., and P. FORBES BORRIE, M.R.C.P. . . . . | 949 |

June 16, 1949

|                                                                                                                |     |
|----------------------------------------------------------------------------------------------------------------|-----|
| Lichen Sclerosus et Atrophicus.—R. T. BRAIN, M.D., and H. HABER, M.D. . . . .                                  | 949 |
| Poikiloderma Atrophicans Vascularis (Jacobi-Lane Type).—BRIAN RUSSELL, M.D. . . . .                            | 950 |
| Acrodermatitis Chronica Atrophicans (Herxheimer).—STEPHEN GOLD, M.B. . . . .                                   | 951 |
| Chronic Moniliasis.—BERNARD A. THOMAS, M.D. . . . .                                                            | 951 |
| Superficial Amelanotic Melanocarcinoma or Precancerous Melanoma.—THERESA KINDLER, M.D. . . . .                 | 953 |
| Lichen Planus Associated with Lichen Nitidus.—H. T. H. WILSON, M.R.C.P. . . . .                                | 955 |
| Punctate ? Petechial Pigmented Occupational Dermatitis.—P. J. HARE, M.B. (for W. N. GOLDSMITH, M.D.) . . . . . | 955 |

(N.B.—The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.)

**Copyright:** The Society holds the copyright of all matter accepted for publication in the *Proceedings*. Requests for subsequent publication elsewhere should be made to the Honorary Editors. All papers, &c., presented at meetings (other than those which have been previously published) are held to be subject to the Society's copyright until a decision in regard to their publication has been made.

**Digests:** Requests for permission to make Digests from the *Proceedings* should be addressed to the Honorary Editors.

All communications concerning Editorial Business should be addressed to  
THE HONORARY EDITORS, 1, WIMPOLE STREET, LONDON, W.1

Applications for advertisement space in the "*Proceedings*" should be made to the Society's official advertising agents Messrs. C. Mitchell & Co. Ltd., Mitchell House 1 and 2, Snow Hill, London, E.C.1.

Copies of the whole *Proceedings* may be purchased through any bookseller. Prices are as follows:—

|                                                                            |                           |
|----------------------------------------------------------------------------|---------------------------|
| Single copies . . . . .                                                    | 10s. 6d. each, post free. |
| Annual subscription, covering 12 monthly issues and annual index . . . . . | £6 6s. 0d.                |

Reprints of Sectional parts may be obtained direct from the Society. Prices are as follows:—

|                               |                          |
|-------------------------------|--------------------------|
| Single copies . . . . .       | 3s. 6d. each, post free. |
| Annual subscription . . . . . | 15s. 0d.                 |

Fellows and Members of the Royal Society of Medicine are asked to apply direct to the Society for any copies of the *Proceedings* they may require, whether whole or Sectional, in addition to those they receive *gratis*. Prices are as follows:—

|                                                                |                          |
|----------------------------------------------------------------|--------------------------|
| Whole <i>Proceedings</i> :                                     |                          |
| Single copies . . . . .                                        | 7s. 6d. each, post free. |
| Complete volume (12 monthly issues and annual index) . . . . . | £5 0s. 0d.               |

|                                |                          |
|--------------------------------|--------------------------|
| Sectional <i>Proceedings</i> : |                          |
| Single copies . . . . .        | 3s. 0d. each, post free. |
| Annual subscription . . . . .  | 10s. 0d.                 |

## Clinical Section

President—G. E. VILVANDRÉ

[April 8, 1949]

### Cardiac Pain Due to Glucose Deficiency. ? Pituitary Dysfunction.—A. SCHOTT, M.D.

Mrs. W. (2653), aged 42.

Complaining of "heart attacks" of which she has had 6 in all during the last three years. They start suddenly and consist of a feeling of intense malaise and pain in the chest, at times severe, sometimes substernal, sometimes in both sides of the chest, lasting one to two hours; not related to exertion. They were diagnosed elsewhere as due to coronary insufficiency. A detailed history revealed that the effect of trinitrin was questionable and certainly not immediate, that, with one possible exception, no attack had occurred within one hour after a meal, that the patient feels in need of frequent intakes of food, that on at least one occasion marked trembling heralded an imminent abortive attack and that glucose seemed to the patient to be the most effective means of stopping an attack. She has always been inclined to sickness in enclosed places; for the last five years she has vomited on such occasions. Indigestion troubled her at times, disappearing suddenly after a few minutes. At the age of 39 the periods stopped shortly after the birth of the youngest of her three children and have not since reappeared. Since then her weight has increased by about 3 st.

On examination (13.10.48).—Overweight (13 st. 2 lb.). Routine physical examination: N.A.D. Blood-pressure 140/80. X-ray examination of the chest: N.A.D.

Resting electrocardiogram: distortion of the S-T intervals and flat T waves in leads 1 and  $V_4$ ;  $Q_3$ : 6 mm. T waves absent in lead aVI. Exercise test (2-step test): marked dyspnoea after 30 ascents carried out in 2 min. 7 sec.; subsequent electrocardiograms showed signs of temporary myocardial anoxia lasting over six minutes after the end of exercise. Glucose tolerance test (Dr. F. A. Knott): See graph (fig. 1). About one hour forty minutes after ingestion of glucose the patient became very pale and greatly distressed; immediate relief by sugared tea and biscuits. Urine: no sugar during test; catheter specimen normal. Wassermann and Kahn reactions negative. Radiological examination (Dr. Friedlaender): no evidence of hiatus hernia or any other abnormality in the gastro-intestinal tract; gall-bladder: slight congenital abnormality, otherwise normal.

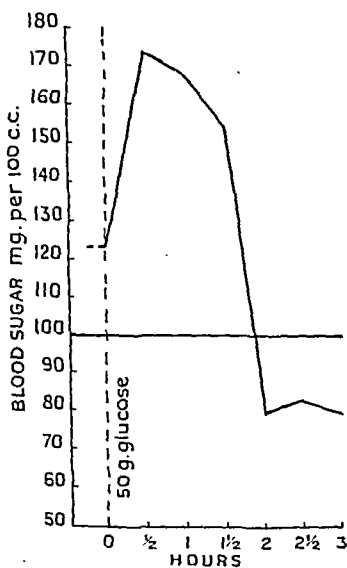


FIG. 1.

meals, each containing as much protein as possible (based on Conn and

Newburgh, 1936) was advised and the patient's progress has been satisfactory.

*Re-examination* (7.4.49).—No recurrence of attacks of substernal pain and only one attack of general malaise after more vigorous exertion about two and a half hours after the preceding meal. Resting ECG. : T waves in leads I and V<sub>4</sub> normal. An exercise test two and a half hours after the last preceding meal showed the same electrocardiographic signs of temporary myocardial anoxia after about the same amount of exercise as before. A further exercise test half an hour after the ingestion of 2-2½ oz. of glucose showed the same abnormalities. The last finding was considered suggestive of, but not conclusive for, additional structural coronary disease.

If spontaneous glucose deficiency is regarded as the precipitating factor of the anginal pain, this case corresponds to those reported by Sippe and Bostock (1933), Weinstein and Mattikow (1939), Harrison and Finks (1943) and Harrison (1944); the last one also showed electrocardiographic abnormalities during an attack.

Conn classifies hypoglycæmia into three types, viz. organic, hepatic and functional. The features of the present case suggest the functional type. The most noteworthy feature was the rapid development of distress and exhaustion during the abrupt fall of the blood sugar. Other aspects, however (onset of symptoms, increase in weight and amenorrhœa after confinement), suggest a pituitary origin, possibly Simmonds's disease, although subnormal blood sugar was not observed either fasting or subsequent to ingestion of glucose, and lactation after the last confinement was normal. Co-existent coronary disease, though rare in women of this age-group (Glendy, Levine and White, 1937; Clawson, 1941), was considered possible, but not proved.

#### BIBLIOGRAPHY

- CLAWSON, B. T. (1941) *Amer. Heart J.*, 22, 607.  
 CONN, J. W. (1940) *J. Amer. med. Ass.*, 115 (ii), 1669.  
 —, and NEWBURGH, L. H. (1936) *J. clin. Invest.*, 15, 665.  
 GLENDY, R. E., LEVINE, S. A., and WHITE, P. D. (1937) *J. Amer. med. Ass.*, 109, 1775.  
 HARRISON, T. R. (1944) *Amer. J. med. Sci.*, 207, 561.  
 —, and FINKS, R. M. (1943) *Amer. Heart J.*, 76, 147.  
 SIPPE, C., and BOSTOCK, J. (1933) *Med. J. Aus.* (i), 207.  
 WEINSTEIN, J., and MATTIKOW, B. (1939) *Ann. int. Med.*, 12 (ii), 1886.

#### Tumour of Bile Papilla Treated by Transduodenal Excision.—FRANK FORTY, F.R.C.S.

S. S., male, aged 60.

*History*.—The patient complained of intermittent attacks of abdominal pain during the past year. The pain started one and a half hours after meals, was sometimes associated with vomiting and was relieved by taking alkalis. It usually started in the right iliac fossa, thence spreading to the centre and left side of the abdomen. On occasions a dull pain was felt in the right hypochondrium. The bowels were regular and no abnormality of the stools was noticed. The patient had never been jaundiced.

*On examination*.—On different occasions slight tenderness was elicited in the right hypochondrium and both iliac fossæ. No abdominal mass was palpable.

*Radiological examinations*.—Barium meal: No abnormality in stomach or duodenum. Barium enema: Slight tenderness over cæcum; appendix not filled; no other abnormality discovered. Cholecystogram: No concentration of dye in the gall-bladder.

*First operation* (laparotomy, 18.1.49).—Adhesions around gall-bladder and appendix. Common bile duct thickened and dilated. No gall-stones found in common bile duct; no obstruction in ampulla encountered by a sound. Cholecystectomy and appendicectomy and drainage of common bile duct.

*Post-operative progress*.—Bile drained freely from the T-tube and the patient's general condition was good but he complained of intermittent attacks of colicky upper abdominal pain and occasionally vomited.



Cholangiogram (27.1.49): No lipiodol entered the duodenum. The shadow of the common bile duct tapered to a point suggestive of an annular stricture. There was no evidence of an impacted gall-stone. The T-tube was clamped at its emergence through the abdominal wall. This was rapidly followed by copious reflux of bile alongside the tube. Cholangiography was repeated on 21.2.49 and again showed complete obstruction of the lower end of the common bile duct, which was dilated as were also the intrahepatic ducts (fig. 1). It was therefore decided to re-explore the common duct.

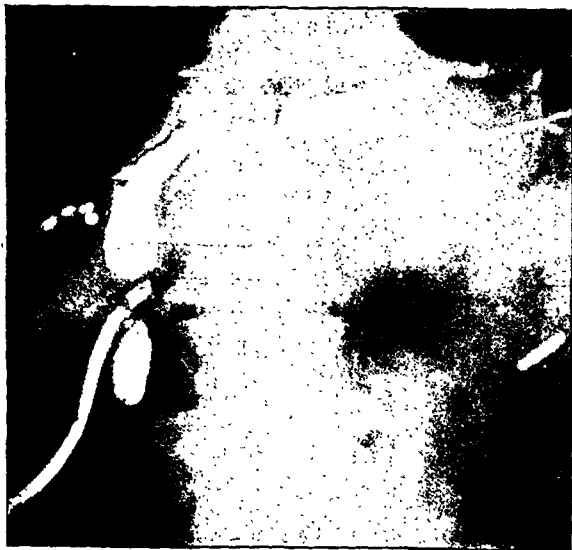


FIG. 1.—Cholangiogram after injection of 10 c.c. lipiodol shows dilated common bile duct and intrahepatic ducts. No lipiodol entered the duodenum, indicating obstruction at the lower end.

*Second operation (22.2.49).*—Common bile duct re-explored—findings negative. Incision of duodenum for inspection of bile papilla revealed soft pink papillomatous tumour, the size of a small cherry. Tumour excised transduodenally. Post-operatively—uneventful recovery and restoration of normal biliary flow.

*Microscopical report.*—Section shows a papillomatous tumour covered by columnar epithelium with a fibromuscular core. Although the general structure appears simple, some of the cells, particularly in the peripheral part of the tumour, show nuclear irregularity, hyperchromatism and occasional mitosis suggestive of early malignant change.

*Comment.*—It is of interest that in this case there was biliary obstruction sufficient to cause dilatation and hypertrophy of the common bile duct without producing jaundice. Presumably, before operation the tone of the common bile duct was capable of maintaining a sufficient hydrostatic pressure to overcome the incomplete obstruction caused by the papilloma. After external drainage of the duct and the establishment of atmospheric pressure within it, these favourable conditions no longer existed and the bile followed the course of least resistance—through the tube to the outside, or alongside the tube when this was clamped. The latent obstruction of the common bile duct was thus revealed.

A further point which invites comment is the early stage, clinically and pathologically, at which, by a rather roundabout process, the tumour was discovered.

The microscopical appearance of the tumour suggests that here, as elsewhere in the alimentary tract, a carcinoma may arise from malignant degeneration in a previously benign papilloma. Furthermore, at such an early stage, when the duodenal mucosa

at the line of section shows no malignant changes, it is reasonable to suppose that the relatively minor procedure of local transduodenal excision of the tumour is sufficiently radical to prevent local recurrence and to forestall the development of metastases.

[Mr. Forty has been asked to report to the Section if there is any evidence of recurrence.]

*Mr. R. T. Burkitt:* I should like to emphasize the importance of waiting for some time between probing the common duct and taking a cholangiogram. We have found that even in cases where no obstruction was present, a cholangiogram taken immediately after probing the duct will be a failure. The sphincter is thrown into spasm and no dye will pass through.

As Mr. Forty has pointed out, the diagnosis between stone and neoplasm in those cases where a small tumour is palpable in the region of the ampulla of Vater is extremely difficult. Probing the common duct is inconclusive; every surgeon must have had the experience of the probe passing down without difficulty while a stone was later found to be present. Biopsy is similarly inconclusive and on more than one occasion we have had a histological report of chronic inflammation, while in actual fact a neoplasm has been the true cause of obstruction.

For these reasons we have completely abandoned probing the common duct in those cases in which we intend to perform a cholangiogram. We have found this a most valuable aid to diagnosis as the appearances of stone and neoplasm are quite characteristic.

### Diaphragmatic Hernia Through the Right Foramen of Morgagni, Causing Asthma.—

LEO RAU, M.R.C.P.

Mrs. M. B., aged 58, first seen 1939, suffering from asthma. This, for no apparent reason, disappeared after three months non-specific treatment. Her husband died in 1942, twenty-seven months after an operation for carcinoma of the bronchus.

This patient was seen again on 30.8.48, after a severe attack of asthma the day before. The clinical examination did not reveal any abnormality in any of her systems. The investigations on this date included full blood-count, E.S.R., and urine; no abnormality was revealed. There was no loss of weight; her blood-pressure was 140/80, pulse 72.

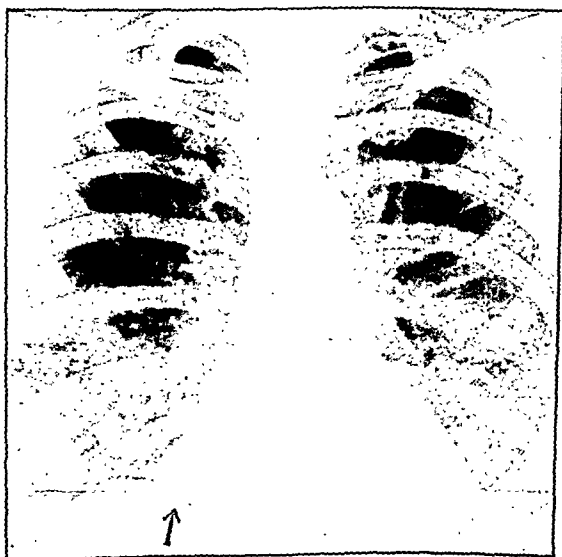


FIG. 1.—Showing shadow in right pericardial phrenic fold.

The radiological examination of the chest (30.8.48) showed a shadow to the right of the heart, above the right diaphragm, in the pericardial phrenic fold, very near the anterior chest wall (fig. 1). The tomogram was very suggestive of a tumour.

Bronchoscopy (Mr. C. Price Thomas, 22.9.48) showed no abnormality.

*Operation* (Mr. C. Price Thomas, 5.10.48).—There was no tumour in the lower lobe of the mediastinum, but a mass in the region of the pericardial phrenic fold which was recognized as being a hernia through the hiatus of Morgagni (between the costal and sternal elements of the diaphragm). The hernia could be reduced easily through the hiatus and the margins of the opening easily palpated.

Since the operation, from which the patient made an *uneventful* recovery, there have been no further symptoms or signs.

*Comment.*—A typical attack of asthma was caused by a right diaphragmatic hernia through the hiatus of Morgagni. Such herniae are not very rare, but, to my knowledge, have never been recognized as a cause of asthma. Operative treatment led to a cure of the asthma.

#### REFERENCE

HARRINGTON, STUART W. (1945) *Ann. Surg.*, 122, 546.

#### ? Strümpell-Marie Type of Spondylitis.—GERALD SLOT, M.D.

A. F. G., male.

History of a fall four years ago when he hurt the sacral region. He was then X-rayed and told that there was *nothing* wrong.

Since then he has had pains and for the last year has had severe headaches. No visual sensations and no vomiting. He complains of backache and pains in his shoulders with a feeling of weakness. There is *no* tenderness.

Neurological examination has been completely negative except for a doubtful extensor reflex in the right leg.

X-rays show sacralization of the fifth lumbar vertebra. At the lower end of the sacrum on the left side (fig. 1) there is a bony outgrowth which was suggested as a

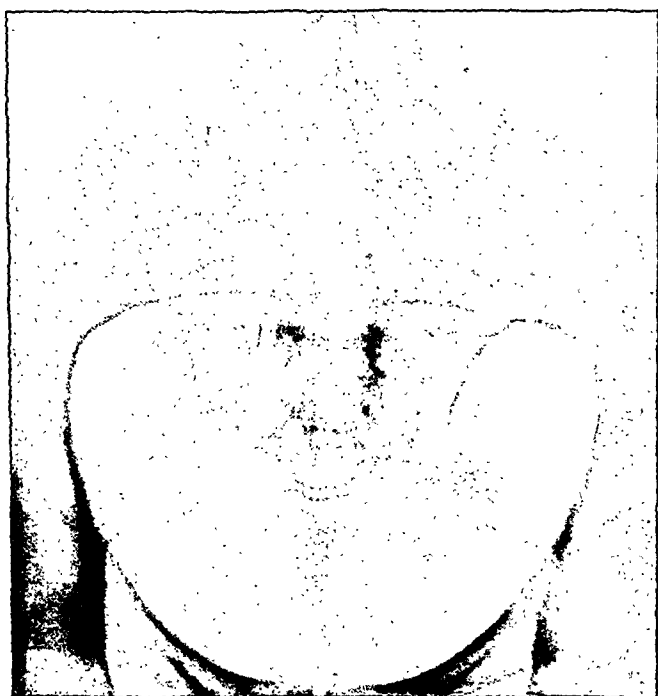


FIG. 1.—Showing ossification of pelvic ligament and sacralization of fifth lumbar vertebra.

possible dermoid, or, by Mr. Dickson Wright, who saw the patient, as ossification of the pelvic ligament.

This case is shown as ? Strümpell-Marie type of spondylitis with ossification of the pelvic ligament. It is not possible to estimate what part his original trauma played in this condition.

Blood-count: R.B.C. 6,160,000; Hb 82%; W.B.C. 5,700 (polys. 80%, lymphos. 20%). No abnormal cells.

**Dr. I. H. Milner:** I suggest that this calcification be termed a "cyclist's bone" in view of the following: It was found in the patient—a cyclist—following a history of local injury in what is probably the great sacro-sciatic ligament. The latter gives origin to fibres of the long head of the biceps femoris and gluteus maximus, both of which muscles are subjected to considerable strain in the case of cyclists. Of the other clinical features of this patient, the character of his pains, the slight asymmetry of his arm-jerks, his raised E.S.R., the haziness on the radiograph in the region of the fourth to fifth cervical intervertebral joint, point to an organic lesion in that area, but I must say that the weakness of his muscles of which he complained was not evident when I examined him to-day.

[May 13, 1949]

### Genito-Urinary Tuberculosis with Extensive Calcification of the Bladder.—

A. ELKELES, M.D.

Male, aged 55.

*Past history.*—Several years previously swelling and purulent discharge from one testicle which healed after treatment. Since 1945 frequency of micturition and slight scalding.

5.11.48: Attended hospital complaining of incontinence of bladder and pain in his back. Preliminary X-ray of abdomen: Nodular calcifications partly coalescent in left kidney region. Large cystic shadow with irregular calcified rim and multiple nodular calcifications in pelvis (fig. 1). I.V.P.: Marked hydronephrosis of right kidney



FIG. 1.—Radiograph of abdomen showing large cystic shadow with nodular calcifications and calcified rim in pelvis. Nodular calcifications forming a ring shadow in left kidney.

with delayed excretion, no excretion from left kidney. Cystogram and retrograde pyelogram: Bilateral hydronephrosis with ill-defined renal pelvis and calyces on the left, bilateral hydro-ureter. The large calcified shadow in pelvis proved to be the bladder.

*Further investigations.*—Blood urea 200 mg.%. Bacteriological examination of urine: Numerous tubercle bacilli. X-ray chest: Diffuse bilateral pulmonary tuberculosis.

*Comment.*—The history and the radiological and laboratory findings are conclusive of long-standing tuberculous infection of the genito-urinary tract. In the terminal stage renal failure and haematogenous spread of the tuberculous infection into the lungs developed. Of particular interest in this case is the extensive calcification of the bladder, since I have been unable to trace any similar radiographs in the literature. It may be assumed that calcification of the bladder is caused by a deposit of lime and phosphates in diffuse ulcerative tubercular cystitis, similar to the rare form of alkaline-incrusted cystitis of non-tubercular origin.

#### Calcification of Ascending Aorta as a Diagnostic Sign of Syphilitic Aortitis.—

A. ELKELES, M.D.

Male, aged 54, complaining of substernal discomfort.

Physical examination reveals a diastolic murmur over the aorta and an Austin-Flint murmur.

X-ray of chest: Enlargement of left ventricle, moderate dilatation of ascending aorta with linear calcification 3 cm. in length at its right border (fig. 1). W.R. positive.

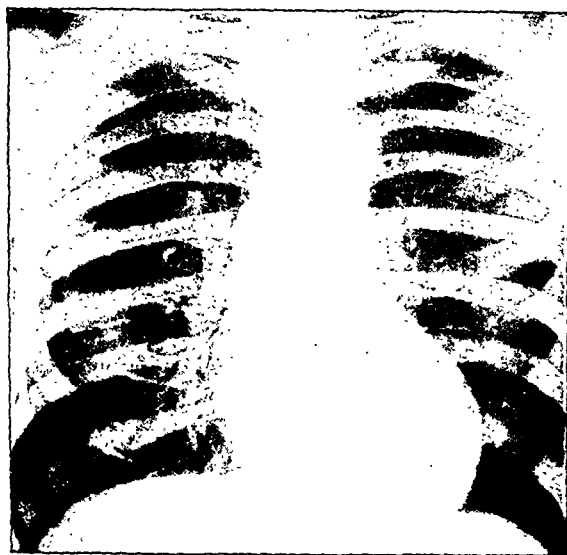


FIG. 1.—Radiograph showing linear calcification at the right border of the ascending aorta.

*Comment.*—Calcification may occur in any portion of the aorta. One of the earliest and most frequent sites is the abdominal aorta. In recently published investigations (Elkeles, 1949) I found in 22.9% radiological evidence of various degrees of calcification of the abdominal aorta in patients over 50. Another common site of calcification in patients beyond middle age is the aortic knob. These findings are generally considered as manifestations of arteriosclerosis. The walls of aortic aneurysms often show calcification, an observation which may assist in the differential diagnosis between mediastinal tumour and aneurysm. Almost no attention had been paid to calcification of the ascending aorta until Jackman and Lubert (1945) were able to show that linear calcification of the ascending aorta is present on radiographs in 22.7% of patients with syphilitic aortitis. Their findings have been confirmed recently by Leighton (1948).

Although there is only moderate enlargement of the ascending aorta in my patient, the marked linear calcification at its right border led me to the diagnosis of syphilitic aortitis. Clinical cardiac findings of aortic regurgitation and the positive Wassermann reaction confirmed the diagnosis.

It is therefore suggested that the detection of linear calcification of the ascending aorta on radiographs should raise the suspicion of syphilitic aortitis.

#### REFERENCES

- ELKELES, A. (1949) *Brit. J. Radiol.*, **22**, 280.  
 JACKMAN, J., and LUBERT, M. (1945) *Amer. J. Roentgenol.*, **53**, 432.  
 LEIGHTON, R. S. (1948) *Radiol.*, **51**, 257.

#### Jejunal Insufficiency with Hypoproteinæmic Œdema.—E. MONTUSCHI, M.D., M.R.C.P.

Male, aged 66. Never been abroad.

1941: Recurrent abdominal pain and bouts of diarrhœa, which have persisted since. Stools are either watery or pale, bulky and offensive. No blood or mucus.

1945: Mild œdema of the ankles. Has since gradually spread, involving the legs and distal parts of the thighs. Some general weakness, but little dyspnœa on exertion. No cough. Appetite fair.

1946: Endoscopic resection of prostate.

*On examination.*—Nutrition indifferent. No obvious anæmia. Tongue rather smooth. Pulse regular. Blood-pressure 130/100. Heart: Apex beat, in fifth space near anterior axillary line; no murmurs. Chest: Clinically clear. Abdomen: Very lax abdominal wall, with little distension; liver not felt. Pitting œdema of the legs. Fundi normal. Knee-jerks present and equal. Ankle-jerks not obtained. Plantars flexor. No sensory loss.

*Investigations.*—Urine: Contained no protein and no casts.

Blood-count: R.B.C. 4,000,000; Hb 80%; W.B.C. 6,400 (polymorphs 74%).

Fractional test meal showed nearly complete achlorhydria.

Stools contained no ova or cysts, and no pathogenic organisms.

Fæcal fat: Total fat 39.6 grammes%; split fat 30.6 grammes %; unsplit fat 9.0 grammes%.

16.12.48: Serum protein 4.7%; albumin 2.9%; globulin 1.8%.

24.3.49: Serum protein 4.8%; albumin 3.1%; globulin 1.7%.

Blood calcium 9.6 mg.%, thymol turbidity 6 units. Alkaline phosphatase 3 units. Circulation time (saccharin) 15 sec. Skiagram of chest showed slight widening of the heart shadow. Electrocardiogram showed low voltage QRS complexes; no other abnormality. Repeated barium meals showed normal stomach, but precipitate passage of barium through the small intestine with loss of normal mucosal pattern. Many diverticula in the small intestine and in the colon.

*Treatment.*—Low fat; high protein; low carbohydrate diet; hydrochloric acid with meals. Folic acid 50 mg. daily for three days, then 10 mg. daily for one week in January 1949. Thiamine 50 mg. I.V. produced no diuresis. Desiccated hog's stomach 30 grammes daily since 10.4.49.

*Progress.*—No improvement with folic acid, but some improvement of diarrhœa and feeling of general well-being on high protein and low fat diet.

Œdema of the legs has diminished, but persists at the ankles. Serum proteins have remained low.

Dr. W. A. Bourne: The presence of a fistula is an accepted mechanism in small intestinal insufficiency, and, in view of the diverticula present in this case, might be considered as a possibility. Diverticulitis produced such a fistula in at least one case I can remember.

Dr. A. Schott asked whether treatment with sulfasuxidine might hold out any prospects, assuming a chronic inflammatory condition of the mucous membrane of the jejunum similar to that of the colon in cases of colitis.

Dr. G. E. Vilvandré said that numerous diverticula of the small bowel were rare in this country, except those found in the duodenal second stage and the duodeno-jejunal flexure, but were somewhat common throughout the jejunum and ileum in America.

Those interested might find a good deal of information on the subject from papers published by J. Cole of Ann Arbor (Michigan) some years previous to the second World War.

Among the many cases described such a condition as jejunal insufficiency leading to hypoproteinemia and oedema might be found to be dependent upon jejunal diverticulosis.

Dr. Montuschi's case was rare and Cole's descriptions well worth investigating and correlating.

Dr. E. Montuschi, in reply, thanked the President and the other speakers for their helpful contributions. Neither barium meal nor barium enema showed a fistula. A low grade inflammatory process of the diverticula would appear to be the cause of intestinal hurry in this case leading to deficient absorption of proteins.

### Typhoid treated with Chloromycetin.—F. MURGATROYD, M.D., F.R.C.P., D.T.M.

C. W. European male, aged 55.

15.4.49: Shivering, sweating, and generalized aching. (This was twelve days after returning to England from a three weeks' tour in Pakistan.)

20.4.49: Attended out-patient department, Hospital for Tropical Diseases. Temperature 103° F., but no focal signs of infection. Hb 90%; R.B.C. 9,430,000; W.B.C. 5,300 (neutros. 66%, lymphos. 31%, monos. 3%); no malaria parasites.

Slight albuminuria.

Admitted to Ward.

21.4.49 to 26.4.49: Remittent fever (101–103° F.). Developed severe toxæmia, delirium, slight cyanosis, distended abdomen, and two crops of rose-coloured spots on abdomen.

21.4.49: Blood agglutinin titre, TO neg., TH 1/250 (Not previously inoculated).

22.4.49: Blood culture, *S. typhi*. Faeces culture, negative.

25.4.49: Blood agglutinin titre, TO 1/250, TH 1/1,000, TVi 1/10.

26.4.49 to 2.5.49: Chloromycetin orally. Initial dose 4 grammes followed by 0.25 gramme two-hourly: total dosage 22.75 grammes.

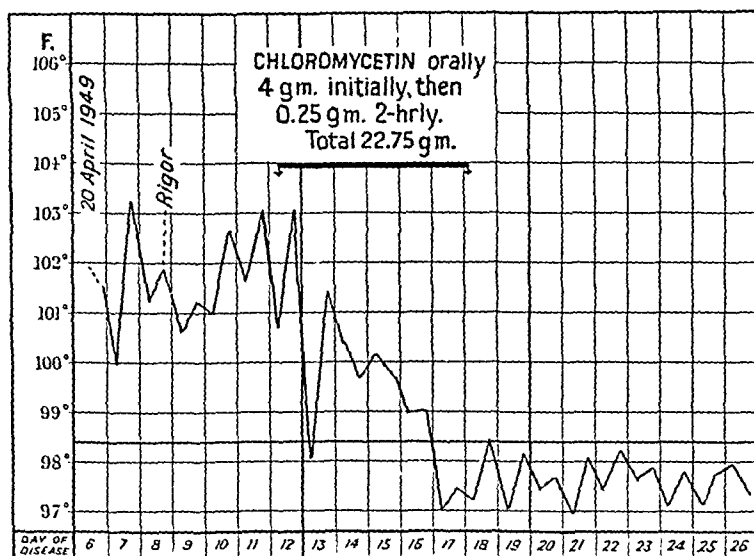


FIG. 1.—Showing effect of chloromycetin in typhoid fever.

During first twenty-four hours of treatment temperature fell to normal; thereafter it rose again and then subsided steadily during next three days (see fig. 1). In the

first twenty-four hours the patient's general condition became markedly worse, then it gradually improved.

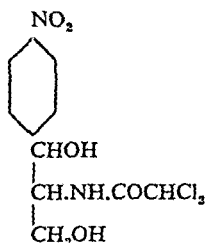
5.5.49: Blood culture, negative. Blood agglutinin titre, TO 1/2,500, TH 1/1,000.

6.5.49: Faeces culture, *S. typhi*.

9.5.49 and 10.5.49: Faeces culture, negative.

9.5.49: Allowed up. Convalescent.

*Comment.*—Chloromycetin, originally isolated from *Streptomyces venezuelæ*, has been synthesized. It is (1)  $\psi$ -1-para-nitrophenyl-2-dichloroacetamido-propane-1-3-diol, a white crystalline substance, with bitter taste.



It has a considerable antibiotic activity against a variety of organisms, including the viruses of lymphogranuloma inguinale, psittacosis, and primary atypical pneumonia, the rickettsias, the enteric, brucella, gonococcal and relapsing-fever organisms, as well as a large number of others.

Chloromycetin is effective orally and, being rapidly removed from the blood, has been given in high initial dosage (50 mg./kg.) followed by 0.25 gramme two-hourly until fever subsides and thereafter for a few days in lessened dosage, although less frequent but higher doses may be equally effective. Therapeutic dosage appears free from toxic effects on man.

An occasional positive stool culture may be found in typhoid after the course of chloromycetin, and sometimes an actual febrile relapse with positive blood culture may occur; such a relapse appears to respond to a further course of the drug.



## Section of the History of Medicine

President—E. ASHWORTH UNDERWOOD, M.A., M.D., D.P.H.

[April 6, 1949]

### The Destruction of John Hunter's Papers

By DUNCAN C. L. FITZWILLIAMS, C.M.G., F.R.C.S.

It is almost impossible to deal adequately with this subject in a short paper because to consider the question of the destruction of John Hunter's papers we have to take the background into account, and in this case the background extends over thirty years.

Hunter died suddenly on October 16, 1793, in tragic circumstances in the arms of Dr. Robertson, without saying a word as he staggered from the Board Room of St. George's Hospital.

The executors of his will were his nephew Matthew Baillie and his brother-in-law Everard Home. Baillie never appears in the matter at all, he had charge of an infinitely better Museum collected by William Hunter. Home was 37 years old and none too well off.

The Museum consisted of ten thousand five hundred and sixty-three specimens of which a considerable proportion consisted of a collection of fossils.

The Museum was a white elephant, Sir Joseph Banks, the President of the Royal Society, reported adversely on it; the College of Physicians refused it bluntly, and finally the Surgeons accepted it, not because of its importance—for that they did not understand—still less did they take it out of respect for Hunter's labours or his memory.

They took it for a very well understood political reason: they had forfeited their Charter at that moment and Parliament had just refused their petition for a new one. Their taking charge of the Museum was to be a means whereby they increased the range and value of their diploma, and hoped to extend it over the whole country; this intention they exploited to the full, and it may be remarked incidentally that the Museum was the making of the College financially.

No catalogue of the collection had ever been made but lists were carefully kept. The papers, which were part of the Museum, consisted of ten large volumes, each devoted to a separate section of the animal kingdom. Hunter treasured these; three of them are near his elbow in the portrait painted by Reynolds. In thirty years he had collected innumerable records of clinical post-mortems, and notes on more than a hundred investigations he had personally carried out—each MS. in a separate fasciculus. There were the MSS. of eighty-seven lectures which he was always altering and adding to. How many animals, birds, reptiles, fishes and insects he had dissected we do not know, but there were notes of them all. Hunter never published monographs, he was only interested in the broad principles of scientific knowledge. It was these papers which Home destroyed as unfit "to be seen by the human eye" [1]. Controversy has raged over the reasons for Home's action ever since. Lately an attempt has been made to whitewash him. Whitewashing is fashionable after the

lapse of time, and we see it in the case of the Borgias, Richard III, and even of Judge Jeffries. Sir Arthur Keith [2, 3], a former President of the College, has set the fashion in the case of Everard Home, and he has been followed, I must say rather timidly, by Dr. Viets [4].

It was this attitude on the part of these writers which was the cause of my interest in the matter.

The Hunters lived at 12, Leicester Square, which had a long narrow garden behind, stretching back to the Castle Street (as Charing Cross Road was then called), where there was another smaller house facing this street. In this the pupils and some of the staff lived. The garden was partly roofed in to house the Museum and the rooms off it where the work was done. The Hunter household was enormous, there were fifty people on the wages roll. Some like William Clift got little besides their keep.

When Hunter died on October 16, 1793, he left nothing. The crash came, Mrs. Hunter and the family moved out, and lived on the sale of the furniture and the Earl's Court Zoo; they were very badly off. The staff was discharged with the exception of the housekeeper, Mrs. Elizabeth Adams, and Clift, who looked after the Museum. His board wages were a shilling a day, and he lived on this for seven years.

The events of the next thirty years must be briefly sketched. As the negotiations between Home, Parliament, and the College of Surgeons were nearing completion after six years, in 1799, Home told Clift to move all Hunter's papers to his house in Sackville Street, which he did.

In 1800 the College took over the Museum and its Court of Assistants appointed a Board of seven curators to look after it. Parliament appointed a Board of Trustees to see that the conditions laid down by Parliament were carried out. One was that a catalogue should be prepared within a reasonable time. The College moved into their new premises at No. 41, Lincoln's Inn Fields, and bought the next house, No. 42, and prepared to build a house for the Museum in the garden.

At the first meeting of the Board of Curators, Home was present as the executor who had hitherto been responsible for it, but he was not a member, as he was not on the Board of Assistants of the College. He offered to produce the catalogue and this offer was gladly accepted.

He was elected to the Court of Assistants in 1803, and at once put upon the Board of Curators which he dominated from that moment.

Clift, in the meanwhile, was employed in preparing the works Home was reading to the Royal Society, illustrating them and transcribing from Hunter's works.

The Board of Trustees met for the first time in 1805 and were shown the preparation made for the reception of the specimens in the new buildings.

In 1806 Clift superintended the removal of specimens from Castle Street, where they had remained while the Museum was being built, to No. 42, Lincoln's Inn Fields.

In 1808 Home reaped the reward of his labours for, by reading innumerable papers before the Royal Society, he had led people to think that the cloak of Hunter as an investigator had gracefully descended upon his own shoulders. This culminated in his appointment as Sergeant Surgeon to the King.

The new Museum was opened in 1813, twenty years after Hunter's death. The same year Home was elected Master of the College, and the Regent made him a baronet.

The Board of Trustees had several time referred to the fact that there was as yet no catalogue and no sign of one being prepared. Again and again Home declaimed that the honour of preparing such a catalogue must be his as executor and as brother-in-law to Hunter. The Board of Curators and Trustees had to be satisfied with these promises, it could not well do otherwise.

Having carefully made sure of his ground, Sir Everard now resigned from the Board of Curators and was at once elected to the Board of Trustees.

In 1821 the Royal College changed its constitution and gave up its civic character, and was ruled in future by a more academic constitution of a President, Vice-Presidents, and a Council. Home was made first President.

In May 1823 William Clift was elected a Fellow of the Royal Society and Home supported his candidature. This fact is significant because there has been some effort to show that there was a long-standing enmity and jealousy between Clift and Sir Everard [5]. But there is no evidence at all that enmity existed between the two men at this time. Home's letters were "dear Clift this," and "dear Clift that" and "Come and read your paper with me

tonight, &c." [6]. What Clift really thought of Home's niggardly treatment of him is not known but nothing appears on the surface.

After the destruction of the papers, things changed—no wonder that Clift overstepped the limits discretion should have dictated, but who can blame him?

In July 1823, Sir Everard drove Clift and Robert Brown in his coach to a Meeting of the Medico-Botanical Society at Kew [3]. On the way down Sir Everard told his listeners that firemen had forced their way into his house as flames were issuing from the chimney, owing to the fierceness of the blaze made by his burning Hunter's papers. Clift knew that the last proofs of the second volume of Home's "Lectures on Comparative Anatomy" had been received back from the printers that week, and that he had drawn extensively on those very papers in the composition of that work.

At this moment Matthew Baillie was lying desperately ill and he died in the following month, never having heard of the loss of the papers.

Clift reported the matter to the Chairman of the Board of Curators, Sir William Blizard, but nothing was done till the Board met in February 1824, when they were all present—Cline, Norris, Sir Astley Cooper, Abernethy, Anthony Carlisle, and Lynn. Clift gave his evidence and said that the papers were an integral part of the Museum, and were essential to the preparation of the catalogue.

A letter was written to Sir Everard on March 5, requesting him to hand over the MSS. which they gathered were still in his possession. Sir Everard replied he had destroyed them all because they were unfinished and "Unfit for the public eye". Further he added that he had extracted from them and published all that was essential, and had closed his thirty years' executorship by destroying them, as Hunter, so he said, had instructed him to do. This seems a plain statement and admission of what use he had made of the papers.

This is the first time in his thirty years of executorship that anyone had heard of either of these reasons from either of the executors.

On March 16 the Board wrote again that they could not believe what his words seemed to imply, and again demanded the remaining MSS. On March 22, Sir Everard wrote that Hunter had made two last requests to him, one that his body should be examined, and the other, that his MSS. should be destroyed.

In the meanwhile Clift, who knew the Sackville Street house well, learned that there were documents which had not been burned. So on April 6 the Board sent a third letter intimating that "they had reason to believe" that he still had some of Hunter's MSS. in his possession and requested him to deliver them up. To this, Sir Everard replied three days later, declining further correspondence with the Board of Curators.

There was nothing further for the Board to do than "with painful reflections but in pursuance of duty" to carry the matter to the Board of Trustees.

Six weeks later the Board of Trustees held a Meeting, ostensibly to consider the preparation of the long-promised catalogue. Lord St. Helens was in the Chair, Mr. Peel and many other eminent individuals attended. Eventually a Parliamentary inquiry was held and evidence was taken, and, as we may suppose, nothing was done or could be done about it. The politicians knew little and cared less for the Museum, or the papers which went with it. It was a mere governmental gesture.

The two excuses Sir Everard used for the destruction of the papers were stated clearly in his first letter, because they were "unfit for the public eye", and because Hunter had instructed him to do so. In the second letter he elaborates this latter reason into a last request by Hunter. Taken together these excuses are absurd, and the one cancels out the other. If Hunter had left instructions that his papers were to be destroyed, then that ended the matter. There was no necessity to mention any other reason. To do so becomes the height of absurdity, if, as Sir Arthur Keith suggests, the reason is to shield Hunter's reputation, for no one had hitherto suggested that they were anything but the ordinary observations and notes of a comparative anatomist. We will, however, take the "reasons" separately, and the latter one first.

A last request, if it means anything, indicates that it was made on the death-bed of the person who made it. Hunter never had a death-bed. The account of his death was as follows: "He (Hunter) went into the next room, and turning round to Dr. Robertson, one of the physicians of the hospital, he gave a deep groan, and dropt down dead" [7]. From the time he was contradicted by someone at the Board Meeting to the time he died, he never said a word. This description is given by Home himself, but Home was not then on the Staff of the Hospital, and therefore was not at the Board Meeting. He had his information second

hand, and the most likely person to have given it him was Matthew Baillie, who was immediately behind Dr. Robertson when Hunter dropped. Home may have been in the Hospital as he was "sent for" but this is uncertain. Therefore we can put aside any idea of a last request.

If he had made the request at some other time, Matthew Baillie the other executor would have known it; what would be more natural than for one or other of the executors to have deplored such a request from Hunter, to someone in conversation, yet for thirty years no one ever remarked that that was to be the fate of the papers. Home says he was to destroy them, but though he does not do it for thirty years his fellow executor raises no objection to the will of his uncle not being carried out. Quite frankly, does this behaviour seem probable or likely? The answer must be "No", so much so, that Sir Arthur Keith does not pin any importance to it, but concentrates on the first excuse and says it was "a pious act" [3] on the part of Home to preserve the reputation of Hunter.

Now the amount of credit we must accord to Home depends on what we think of the honesty of his excuse. Let us see if he is acting honestly in the matter of the papers anywhere. The firemen forced their way into the house and saw the holocaust of papers, and we must presume they either put out or limited the blaze. It is very unlikely that Home persisted in banking up the fire with the other papers. The servants must have come in with the firemen, and they knew and probably told Clift that there were many which were not burned. Home never said he made a second fire of the remainder, yet he says and repeats that he burned all, and when the Board of Curators write their third letter saying they think he still has some in his possession, he does not deny it, but refuses to discuss the matter further.

Yet on two subsequent occasions he produces bundles of post-mortem reports to the Board of Trustees. These have been looked over by my colleague Mr. Zachary Cope, who unearthed an excellent account of a death from a ruptured appendix from among them. I believe it is the earliest on record. But these post-mortem reports had no bearing whatsoever on his own work of "Comparative Anatomy", so there was no necessity to destroy them. That Sir Everard had been foxing becomes still more evident when his son, Sir Everard Home, Captain of H.M.S. *Racehorse*, six years after the death of his father, handed to the President of the College, Robert Keate, the entire folio on the Natural History of Vegetables, and ten separate MS. fasciculi. Again seven years later when he attended to hear the Hunterian Lecture in 1839 by Edward Stanley, he delivered a sealed packet which proved to be the entire folio volume on the fossils. From this folio we learn that Hunter was forty years ahead of the geologists of his day.

What now becomes of Home's contention that he was instructed to destroy the papers? In the first place, the papers belonged to and were a part of the Museum as bought by the nation, though he had taken the precaution of having them removed to his own house before the College officially took over the Museum. If they were to be destroyed, then was the time to say so, and to carry out the wishes of their author. Secondly, he kept them for thirty years, using them to prepare most of the hundred and more papers he read to the Royal Society during that time. Lastly, and perhaps most significantly of all, he did not trouble to destroy those papers which had no bearing upon what he himself had been writing.

The list drawn up by William Clift of the papers read by Home mostly to the Royal Society are 143 in number. No person had ever read such a wealth of papers on such a variety of subjects before. Now apart from one or two dealing with the actions of drugs such as colchicum they all deal with the animal kingdom, except six which refer to fossils.

Apart from these he takes no further notice of the fossil world. He is not interested either in the vegetable kingdom. It is with the animal kingdom that the vast bulk of Sir Everard's papers deal. A large number are monographs on separate animals. It is surely significant that the papers dealing with the animal kingdom were all destroyed, the others were found intact.

So much then for the first excuse, now for the second that what had been written was "unfit for the public eye". This can only mean what Sir Arthur Keith thinks it means, that Hunter's views were so atheistical, to put it bluntly, that to publish them would call down upon his memory such obloquy and odium that it might involve the reputation of his executor. Keith says Sir Everard was conventional and orthodox in his beliefs and considered "he was doing his old and wayward master a true service when he destroyed his unpublished MSS." "It was vain stupidity—a dangerous possession—rather than criminality, which lay at the roots of Sir Everard Home's crowning act of vandalism". [3].

If this suggestion is investigated we find incontrovertible evidence that such a hypothesis cannot be entertained for a single moment. It is highly unlikely that in any of Hunter's notes on the dissections of the numerous animals that he investigated there could be anything calling in question the powers of the Supreme Being. Yet these were the very works which were all destroyed as being "unfit for the public eye".

Where the orthodox faith in the literal meaning of the Written Word might be called in question would be in dealing with prehistoric things such as fossils, but these were the very things which were not destroyed. Moreover, if these papers are studied it will be seen that Hunter in no way runs counter to the usually accepted beliefs of his day, which were literal in the exact sense of the word. On the contrary, he tries to support them, and when he cannot do this as a scientific man, he remains silent, in no case does he attempt to controvert them.

This is amply shown in his dealing with the story of the Creation in his *Introduction to Natural History*, for he seeks even there to find an underlying scientific arrangement for what is done, and approves the Lord's idea of starting with the simplest things and working gradually up to the highest, namely man. For Moses he says "divides the labours of the six days very naturally. The first two were employed in the formation of the globe, and everything relating to it. Then on the third day the earth brought forth grass, &c., yielding seed of its own kind. On the fifth day the waters brought forth fish and fowl; and on the sixth day the earth brought forth the beasts of the earth; and last of all man was formed. Now this is a natural rise or progression from the most imperfect to the most perfect".

Here Hunter is preaching exactly what Genesis taught. What he did see at once, and what any discerning person would notice was that the day and night were created on the first day, but that the sun and moon which made them were only created on the fourth day. Here Hunter probably could not accept this sequence but does not attempt to shake the public faith in it. In place of criticizing the Sacred Writings, he simply sidesteps the fourth day completely and does not mention it. Is this, we may ask, the act of an atheist?

"Moses", Hunter continues, "has been more particular in his account of man than of any other creatures, but from him, it would appear that only one man was formed in the supernatural way he describes. Yet, from the history, we are naturally led to suppose that there were more, either produced, or existing at that time, as Cain went to another part of the globe and got him a wife."

In dealing with the Flood he seems even more explicit for he says: "The same history brings us much nearer viz. the Flood, where it is positively asserted that every living thing was drowned, except seven of each species that were clean and two of every sort that were unclean. And likewise that there were but one man, his wife and off-spring saved. Later historians have thrown but little light upon this subject, and many have only endeavoured to make the present appearances clash with the account given in the Old Testament." If language means anything, it is obvious that he is not among those to whom he refers in his last sentence.

In the folio of fossils which survived the fire, he speaks again about the Flood, and says that forty days' submersion is not enough to account for all the fossils found on dry land, as the marine animals would have only been left upon the surface of the earth. "But it would appear that the sea has more than once made its excursions on the same place; for the mixture of land and sea productions now found on land is proof of at least two changes having taken place". Hunter does not question the story of the Flood, all he does is to imply that there was more than one flood, though the Bible only mentions one.

These quotations could be multiplied many times, but I hope I have said enough to show that there is nothing in the works of Hunter which controverts the scriptures, or is "unfit for the public eye". Taking these quotations into consideration it is surprising that Sir Arthur Keith says that John Hunter "silently and resolutely thought and wrote as if the book of Genesis had never been in existence" [2].

Additional presumptive evidence that Hunter was not an atheist may be adduced from his relations with the Clerical Profession. One of his favourite pupils was William Henry Matthew, son of the Rev. Henry Matthew of St. Martin-in-the-Field, who read the burial service over Hunter when he was interred there. There was another pupil who lived in his house, Thomas Nicol, who was the son of a parson [8, 9]. Now the fathers of these two would hardly have committed their sons to his care if there had been anything atheistical in his views.

One of the closest friends of the Hunter family was the Rev. Robert Nares, a Westminster School mate of Home's and a great friend of Mrs. Hunter. He was later Archdeacon of  
Nov.—HIST. OF MED. 2

Stafford and Canon of Lichfield. It was Nares who bore to Anne Hunter Walpole's regrets on learning the death of her husband. He afterwards wrote her obituary notice in the *Gentleman's Magazine* [10]. Hunter seems to have been partial to clergymen for he never would take a fee from those in Holy Orders.

Considering the unpopularity of John Hunter among his jealous colleagues, we can presume that if he had been a free-thinker as Keith supposes, the fact would have been blazed abroad to his detriment. Yet no one has ever traced insinuations of the kind to any of Hunter's contemporaries.

Keith has surely pressed the case for Hunter's unorthodoxy too far as clearly shown by two of his statements.

In the first he remarks: "There were in his (Hunter's) writings statements which would have made the hair of the orthodox stand on end if *all* his works had been published in 1793." But he fails to mention a single example or to give any reference to the writings he has in mind.

In the second he is even less convincing when he writes that Home "saw the *dire fate which overwhelmed* William Lawrence when he spoke out his true thoughts" concerning man's relationship to animals in the theatre of the College in 1816 [3]. Here an utterly false impression is given to those who are not conversant with the history of William Lawrence. Lawrence published his lecture in book form and the book caused some stir in ecclesiastical circles, and he lost a lawsuit over its copyright. But his remarks had no scientific or philosophic importance, and were regarded as made in an attempt to startle his audience.

Lawrence besides being lecturer at the College was a surgeon and lecturer at St. Bartholomew's Hospital for thirty-three years, examiner at the College for twenty-seven years, President of the Medico-Chirurgical Society in 1831, President of the College in 1846 and again in 1855. He was a man of such influence that he was rarely opposed on the Board of the Hospital, had an extensive practice, twice delivered the Hunterian Oration, was appointed Surgeon-Extraordinary and in 1857 Sergeant-Surgeon to the Queen, and lastly created a baronet in 1867. Many surgeons must have envied the dire fate that Sir Arthur says overwhelmed him.

For the reasons I have given I find untenable Keith's views on Hunter's religious beliefs as the mainspring of Home's actions in burning the papers and I have felt bound to controvert them.

#### REFERENCES

- 1 Rpt. Parliamentary Commission Pt. 2. Q.5053.
- 2 KEITH, A. (1928) Bicentenary of John Hunter, *Nature*, 121, 210.
- 3 — (1923) Vicary Lecture on the Life and Times of William Clift, *Brit. med. J.* (ii), 1127.
- 4 VIETS, H. R. (1930) The Destruction of the Hunter Manuscripts, *Bull. Johns Hopk. Hosp.*, 46, 145.
- 5 OPPENHEIMER, J. M. (1946) New Aspects of John and William Hunter. London, p. 57.
- 6 HOME, E. (1805-40) Letters to William Clift (Library, Royal College of Surgeons).
- 7 — (1794) A Short Account of the Author's Life, in Hunter, J. A Treatise on the Blood, Inflammation, and Gun-shot Wounds. London, p. lxi.
- 8 PEACHEY, G. C. (1924) A Memoir of William and John Hunter. Plymouth, p. 15.
- 9 FINLAYSON, J. (1890) Account of a MS. Volume, by William Clift, relating to John Hunter's Household and Estate; and to Sir Everard Home's Publications, *Brit. med. J.* (i), 738.
- 10 NARES, R. See NICHOLS, J. B. (1817 onwards) Illustrations of the Literary History of the 18th Century, 7, 638.

## Section of Neurology

President—WILLIAM JOHNSON, M.C., M.D., F.R.C.P.

[December 2, 1948]

### Somatic Movements of the Prematurely Born Fœtus—Film Demonstration

By IVY MACKENZIE, M.A., B.Sc., M.D., F.R.F.P.S.

A NUMBER of films were shown from a series taken to demonstrate successive phases of development of the prematurely born fœtus as these were revealed in the emergence of somatic movements. The cases comprised fœtuses delivered at the end of five, six and seven months' gestation. One, born at five months, survived fifteen months and another, born at six months, had developed normally into a childhood of five years. The remainder lived over periods from two hours to two weeks.

Dr. Mackenzie explained that the construction of the nervous system proceeded according to a time-table, and a standard of reference was made in serial sections of the central nervous apparatus from specimens of five, six and seven months' gestation. These were stained for myelination, the course of which revealed, to some extent at least, the trend of events which mark the relation of structure to function. It was only in a general sense, however, that myelination provided a clue to potential function. Impulses were conducted by fibres before they became myelinated and also by fibres which had become demyelinated through disease; and there were also fibres which never became myelinated. But the ontogenetic process as a whole did take place according to "fundamental laws" which were first formulated by Flechsig.

While the main purpose of the demonstration was to call attention to some features of functional activity, it was well to bear in mind the general structural background as revealed in myelination:

(1) Fibres with a common function became myelinated approximately at the same time and the order in which the various systems matured may be, as had been pointed out, set forth in a time-table. Thus the vestibular fibres which had to do with the tonicity of the somatic muscles myelinated about the middle of the intra-uterine period while the pyramidal fibres acquired their myelin in the first year after birth.

(2) The order of myelination followed generally that in which the neurites emerged from the neuroblasts. Thus in the case of the spinal nerves the motor neurones matured before the sensory elements. The neurites from the anterior cornual cells had already reached the myotomes before the spinal ganglia were connected to the cord. The connector or interstitial neurones in the medulla and cord myelinated early, possibly prior to the afferent connexion.

(3) The sequence of myelination from one system to another in the human brain and cord represented generally a recapitulation of the phylogenetic history of the vertebrate nervous system as a whole. Thus, those parts of the nervous system which were common to the vertebrate phylum and served the same purpose, such as the oculo-motor nerves, the posterior longitudinal fasciculi, the posterior commissure, the vestibular nerves and the internuncial zones, were the first to be myelinated in the human subject. At the end of the fifth month of fœtal life these were the tracts which, in addition to the peripheral, motor and sensory nerves, stood out prominently in the picture of myelination and they comprised that portion of the neural apparatus to which were assigned the activities displayed in the pictures shown.

The infant born at the end of five months had still about another five months to live before myelination began in the pyramidal tracts and a corresponding delay was noted in the ontogenesis of the corpora striata in the higher vertebrates. Each of these nuclei comprised two distinct bodies which differed fundamentally both in structure and in function.

The pallidum or paleostriatum was the older phylogenetically and appeared in the lower vertebrates as a motor centre in relation to the vegetative centres in the hypothalamus. The other portion, the neostriatum, including the putamen and caudate, appeared later in relation to the evolution of the neopallium or cerebral mantle, and had to do with the wider range and variety of movement which that expansion implied. The course of myelination in the corpora striata in the human subject reflected the intrinsic sequence of events in the evolution of these bodies. Already in the sixth month of foetal life there was evidence of myelination in the pallidum and at full-term birth the fibres which connected the pallidum with the thalamus and hypothalamus were for the most part myelinated, whereas those which entered the pallidum from the putamen or neostriatum were still without myelin. It was thus reasonable to assume that the infant prematurely born at five months or six months, or later, was a "thalamo-pallidal creature" and that the somatic movements which it executes such as breathing, chewing, swallowing and excretion, as well as other incidental movements like grasping, kicking, movements of the eyes, of the head and neck, and movements of expression may all be ascribed to the early development of the neural apparatus in the more caudal part of the brain-stem and spinal cord.

The prematurely born foetus was suddenly subjected to the tests of an abnormal environment. Deprived not only of maternal nutrition but of the security and warmth of the amniotic medium it had to fend for itself. To survive it must breathe, swallow, digest and excrete and the internal *milieu* must be such as to provide for the maintenance of an equable temperature. Survival depended on the fact that the vegetative system took precedence in the process of development; and its somatic components were the first to exhibit the regular and orderly activity of striated musculature. The muscles of breathing, sucking, swallowing and excretion exercised a physiological function in the sense that they served an organic purpose and contributed to survival, whereas the movements of the limbs, of the head and of the eyes were irregular and purposeless so far as serving the immediate requirements of the organism was concerned. This, of course, obtained also in the case of the foetus born at full term but it was possible to discern in the prematurely born foetus from five or six months onwards special activities and reactions which emerge in a more or less regular way in the course of development and may thus be taken as an expression of the progressive construction of the central nervous system. Outstanding among these were activities and reactions described by the experimental physiologists, such as "grasping", "pedal rhythm" and the "neck reflexes" of Magnus and de Kleijn. These were in themselves phenomena of significance inasmuch as they demonstrated the validity of the conclusions based on the experimental methods devised to demonstrate the function of the nervous mechanism by operative interference with its component parts.

*Case 1.*—Born spontaneously at the end of five months' gestation (calculated according to menses). Length from vertex to heel 12 in. Weight 13½ oz. Nails on all fingers. Nails on large toes, just visible on other toes. Respiration 40 per minute. Pulse 150 per minute. Attempts to cough and sneeze as if to clear air passages. Fed with a pipette for the first week and swallowed freely. From the end of the first week, when a small teat was procured, it sucked from a bottle. Meconium passed from bowel. Abdominal distension relieved on fifth day by injection of 2 drachms of olive oil followed by ½ drachm milk of magnesia by the mouth. Bowel and bladder sphincters active from birth.

The infant was covered with olive oil, kept in cotton-wool and placed between hot water bottles in a room of varying temperature but comfortably warm. It was not in hospital. Weight at birth 13½ oz.; tenth day 17 oz.; fourteenth day 20 oz.; at the end of ten weeks 3½ lb. When it had reached the age of full-term birth its weight was 6½ lb. For the first three months its only food was diluted cow's milk with an occasional addition of a few drops of cod-liver oil.

*Somatic activities at birth.*—Respiration, sucking, swallowing, extension of head and neck with occasional turning and bending, flexion at elbows with tendency to retraction at shoulders, slow writhing and wriggling movements of the body with adduction of the lower limbs and occasional flexion. At birth the eyelids were closed; they opened on the fifth day when the olive oil was injected into the bowel. Conjugate movements of the eyes were noted when the eyelids opened.

*Grasping.*—In the first days after birth the fingers clasped on placing a small rod in the palm. Two months later the hand grasped sufficiently firmly to enable the body to be moved from side to side. It was noticed that the grasp was more easily elicited in the hand which was uppermost when the body was lying on the side, that is to say, with the body on the left side the right hand showed the firm grasp.

*Neck reflexes.*—These occurred spontaneously and could be elicited two months after birth.

*Stepping.*—Two months after birth, with the body suspended, held up by support under the armpits, firm stepping occurred. When the body was lowered so that the soles of the feet touched the ground, the limbs became firmly extended as if "standing" had taken place.

*Eye reflexes.*—Ten weeks after birth the pupils responded to light though there was no other ocular reaction to light. There was at this stage no response to noise. Six months after birth the eyes followed a moving light and three months later the hand was put out to grasp an object in the field of vision.



With some slight retardation development progressed normally over a period of fifteen months when the infant died from pneumonia. At the end of this time it was able to creep and crawl and its emotional and social reactions were characteristic for a child of 9 or 10 months.

*Post-mortem* examination showed a well-developed brain. Although the convolutions were somewhat abnormal the pyramidal tracts were well myelinated; the spinal cord showed no abnormality.

*Case 2.*—Delivered spontaneously at the end of five months. Length 11 in. Weight 1 lb. After birth there was an occasional gasp but as these appeared to cease it was placed in cotton-wool to be preserved for anatomical examination. On removal from the cotton-wool it was seen again to gasp and on being exposed to heat it began to breathe at a rate of 30 per minute, the pulse being 140 per minute. The head and trunk had acquired a firm axial posture. The first film was taken three hours later. The movements resembled those in Case 1—slow writhing and wriggling with extension and flexion of the arms and legs. All reflexes, including movements of the tongue and sucking, were easily induced. It was able to swallow. It continued to breathe and show other vital activities for six hours when rhythmic breathing was replaced by gasping. Exposed to heat again the breathing returned. The film taken at this stage resembles the earlier one. The infant died seventeen hours after birth.

*Case 3.*—Delivered by Cæsarean section at the end of five months. Length 12 in. Weight 1 lb. Occasional gasping. No respiratory rhythm or capacity to suck. Placed on its back the lower limbs were elevated by flexion at the hips. On changing the position, or shaking the body, alternate movements of the limbs occurred. On further raising one of the limbs with a rod below the knee, the other limb showed rhythmic flexion with some adduction at the hip. Rhythmic contractions took place with the limb free in the air—the contractions were predominantly flexor and at the hip. Stimulation of foot or hand was followed by "lightning reflexes" in other limbs. All this occurred in the absence of respiration.

*Case 4.*—Delivered by Cæsarean section. No breathing, but occasional gasping. Movements similar to those in Case 3 except that instead of alternate rhythm in the lower limbs, the flexions were simultaneous in the two limbs (gallop rhythm).

*Case 5.*—Delivered spontaneously at the end of six months' gestation. Film shows "neck reflexes". Survived two days.

*Case 6.*—Delivered by Cæsarean section at the end of seven months' gestation. Weight 3 lb. Lived fourteen days. Showed "neck reflexes" and firm pedal rhythm on being held suspended in the air.

*Case 7.*—Delivered spontaneously at the end of six months' gestation. Length 15 in. Weight 2½ lb. The course of events in this case as shown in the film is a recapitulation of what was seen in Case 1. Neck reflexes, grasping reflexes, firm pedal rhythm, were seen in the earlier phases. On reaching an age corresponding to full-term birth the eyes turned to a moving light and four months later the hand was put out to grasp an object. From an age corresponding to 8 months onwards it crept and crawled and at the stage corresponding to 1 year was able to stand at a chair supported with one hand and play with a toy with the other. A month later it was able to walk, to get up from the floor and to take off and put on its shoes. The later course of events corresponded with that of the development of a child born at full term and it was alive and well at the end of five years.

The most dramatic feature of survival from early premature birth was the persistence with which the organism preserved its identity and the consistency with which it pursued its course towards maturity, and all this in spite of abnormal environment. The process of construction and the emergence of function proceeded according to time-table. The course of events would seem to be directed by an "inner drive", a destiny in the design of nature.

No less striking was the efficiency with which the vegetative system operated on premature delivery, even at five or six months. This derived, no doubt, from phylogenetic inheritance which secures, at an early date, a complete development of the tegmental and spinal structures essential for respiration, alimentation and excretion. Breathing and swallowing are subserved by a common mechanism in the substantia reticularis so differentiated that from the start they operate in harmony and in mutual exclusion. There was no disorder such as coughing or sneezing or hiccough or vomiting which mark the derangement of these mutually integrated though independent activities. Whether, and if so in what sense, the "pedal rhythm" and "neck reflexes" were indicative of an "inner drive" is a matter for further investigation. In any event the rhythmic movement of the lower limbs at five months did suggest an intrinsic rhythm comparable with that described by Graham Brown, whose experiments led him to conclude that there is a "rhythmic centre" in the lumbo-sacral enlargement comparable with the "respiratory centre" in the medulla. It did not in the least detract from the value and importance of the Sherrington School in the elucidation of the structure and function of the nervous system from the point of view of reflex activity, to suggest that there were other factors of an inherent character such as "intrinsic rhythm" which contributed to the activity of the system as a whole.

What had been shown and said was but a brief outline of research in the pursuit of which Dr. Mackenzie said he owed a debt to the interest and encouragement of Sir Joseph Barcroft and to the publications of Preyer, Minkowski, Windle, and other pioneers in the field of foetal physiology.

[April 7, 1949]

Chairman—C. WORSTER-DROUGHT, M.A., M.D., F.R.C.P.

## A Review of Cerebral Angiography

By JAMES W. D. BULL, M.D., M.R.C.P., D.M.R.

THE name of Moniz will always be associated with cerebral angiography. He introduced the method in 1927 and by October 1931 had performed 302 arteriographies, using 25% sodium iodide as a contrast substance. After this he started using thorotrast which is painless and does not produce arterial spasms, but none the less has certain disadvantages. Some Germans, notably Löhr and Riechert, took up the work, but in Britain and America it was little used in the nineteen-thirties. In Scandinavia it was used to some extent, but was subsidiary to pneumography. Thus for many years there were two schools, one following Moniz and the other following Dandy's discoveries of pneumography, and the two schools were poles apart, each regarding its method as the better in the diagnosis of intracranial lesions. Then in 1944 a virtual revolution occurred. The Norwegians, Engeset and his co-workers, developed the percutaneous method and placed it on a routine footing. Furthermore they established the value and safety of the iodine-containing contrast medium, diodone, which was already being used in U.S.A. for open surgical arteriography. The Norwegians were not the first to use the percutaneous method. In 1927 Moniz tried four times unsuccessfully and so resorted to the open method. In 1936 Loman and Myerson in the U.S.A. described the method but it never became a routine.

For any investigation in medicine to become routine it must be safe and relatively simple and have the patient's co-operation. This could never really be said about open arteriography. Naturally no patient willingly submits to an operation which is not therapeutic. Besides this many patients, particularly women, do not like wearing a scar on their neck for the rest of their lives. The pioneer work of the Norwegians, quickly followed by the Swedes, Lindgren and Wickbom, has firmly established the percutaneous method and put it on an equal footing in radiology with, let us say, intravenous pyelography.

Those who are not intimately acquainted with this investigation will have certain questions in their minds, the answers to which I will attempt to give.

*Safety.*—The dangers are very small and compare favourably with ventriculography and encephalography. Out of some 500 odd cases I have experienced, three patients have died within two days, but arteriography was not proved to be the cause in any of them. The first was a man with a large frontal astrocytoma. Having been quite co-operative and punctured under local anaesthesia, he went into coma rapidly about two and a half hours after arteriography and died the next day without regaining consciousness. Dr. J. G. Greenfield could find nothing at autopsy related to the arteriography. The most striking feature was the considerable coning of the uncus. This man had a large inoperable tumour and his uncus would have coned through the tentorium ultimately, but it seemed more than a coincidence that it happened two and a half hours after the arteriography. A paper published by Broman and Olsson (1948) may explain the cause. The second case was an elderly subcomatose woman with high papilloedema and mental changes. There were no localizing signs and we thought she might have a large frontal or possibly cerebellar tumour. As she was unable to co-operate I decided to perform the angiography under general anaesthesia. She received some basal narcosis as well, and was not a very good colour under anaesthesia. Arteriography showed a wideswept anterior cerebral artery situated in the mid-line, thus suggesting a posterior fossa lesion. She never recovered consciousness and died the next day. An autopsy was refused. Death might have been due to the arteriography; it might have been the anaesthetic; it was probably a combination of the two. In the third case the patient had a fatal haemorrhage into a tumour two days after angiography. Again nothing relevant was found at autopsy. One patient developed an aphasia and partial monoplegia which began to recover the next day, and after a few days, recovery was complete.

Occasionally a slight pyrexia is seen for two or three days associated with a very sore neck. This is probably due to some saline or contrast substance or both having entered the carotid sheath and to the small haematoma which sometimes develops. This can occur when the lumen of the needle is not perfectly in situ in the vessel. As one becomes more skilled in the technique of puncture this complication is unlikely to occur in any but the most difficult

cases. Generally speaking the method causes no worries or unpleasantness to the patient or operator. I have never seen a hæmorrhage from the artery sufficient to cause worry. About one minute's digital pressure after removing the needle is all that is necessary. I often ask patients whom they dislike more, me or the dentist. Some say one, some say the other, but a better test is that very few patients need any persuading to return to have the other side injected or for a repeat arteriography after treatment. If everything is explained to them beforehand they take it very well.

*Sensitivity to the drug diodone*<sup>1</sup>.—This can be a great problem and worry or no problem at all, depending on the radiologist's approach. Intravenous pyelography, where the same drug is employed, is carried out daily at nearly every hospital and tens of thousands of such examinations are made annually, nearly always *without* sensitivity tests. Severe reactions and deaths are almost unknown. Should one therefore test the patient's sensitivity? If the test were certain and foolproof one would say "yes", but there is evidence to suggest that a small dose given intravenously or intra-arterially can cause no ill-effects, while very, very rarely a large (normal) dose will cause a severe reaction or even death. For this reason I say it is a very difficult problem, or no problem at all.

*Premedication and anæsthesia*.—In my view it is very desirable that the patient should be conscious. He will nearly always co-operate well, keeping still while the pictures are being taken. He can assist the operator by describing his sensations and he can say if he is not feeling well. An anæsthetic is an added risk, though admittedly negligible, and an already quite large and space-consuming team and equipment is made larger by the anæsthetist and his apparatus. I only ask for an anæsthetist's help in children under 15 or so, or for unco-operative patients. Premedication is largely a matter of personal choice, but omnopon  $\frac{1}{2}$  gr. (20 mg.) is usually suitable. The patient should be starved for at least four hours and preferably have the procedure explained to him on the previous day by the operator, to gain his confidence. A few c.c. of 1% novocain is given as local anæsthetic.

*Technique*.—Lindgren (1947) has described the technique most comprehensively. The important factor is an experienced team used to working together. With regard to the actual puncture of the artery, Turnbull (1939) says: "Direct puncture of the common carotid artery is not a formidable procedure, but neither is it easy." Most operators do not feel the master of the artery until they have done about 50 cases, and after that the artery is the master only about once in 100 cases. Small children, whose necks are very short and whose carotids are very mobile, are the most difficult cases in my experience. The operation can suitably be performed on out-patients, but they should go to bed or rest for a few hours afterwards.

The arterial puncture takes from a few seconds to many minutes, but usually not more than two or three minutes. Normal saline is then injected until one is ready for the radiographic exposure. 10 c.c. of contrast are injected and three pictures are taken at two second intervals. The patients experience a feeling of warmth in the distribution of the artery and they will indicate the exact area. Lateral pictures are usually taken first, then the tube is shifted into the antero-posterior position and the procedure repeated. This all takes about four or five minutes. If stereoscopic pictures are desired, two sets of laterals and antero-posterior views are taken, making the appropriate shift of the X-ray tube. No amount of stereoscopic views will substitute for views in two right-angled planes. Saline is injected again until one has seen the pictures and decided if further views are necessary. This takes another six or seven minutes, so that a case normally takes fifteen to twenty minutes in all. Supplementary projections such as oblique and basal views are taken if indicated.

*After-effects*.—A few patients feel sick and a small proportion of these are sick, but most have no after-effects at all, except a slightly sore neck for a day or two. The vomiting is caused by the contrast drug and is also seen in intravenous pyelography.

*The radiographic results*.—The percutaneous results are better than the open method for various reasons. The most important is that once the needle is well in situ it is held firmly by the arterial musculature and the subcutaneous tissues—so firmly that the operator need not hold the needle all the time, only during the injection of the contrast. With the open method it is very difficult to keep the needle in the artery for any length of time. There are far less towels and paraphernalia around with the percutaneous method, so that accurate

<sup>1</sup>Diodone is the pharmacopœial name for the diethanolamine salt of 3 : 5-diiodo-4-pyridone-N-acetic acid. It is marketed as Pyelosil, Glaxo. In the U.S.A. it is called Diodrast; in Scandinavia, Umbradil; and in Germany, Perabrodil. It is issued in three concentrations: 35, 50, and 70%. The last should never be used for cerebral angiography, and the 50% solution should be avoided if possible. This substance as used is harmless to the tissues and should not be confused with Iodoxyl (Pylectan; Uroselectan B), which is the disodium salt of N-methyl-3 : 5-diiodo-4-pyridone-2 : 6-dicarboxylic acid and is issued as a 75% solution.

centring of the X-ray tube is much easier. Furthermore the patient is nearly always conscious—a great advantage.

**Protection against radiation.**—Careful protective measures against radiation striking the operator's fingers must be taken. This is particularly important when surgeons undertake the work, as their fingers are more valuable than those of other doctors, and they may not know that they have damaged their fingers until several years later.

#### THE SCOPE OF CEREBRAL ANGIOGRAPHY

**Anatomy.**—A thorough understanding of the normal anatomy and variations is essential as a basis for arteriographic interpretation. This subject is not satisfactorily covered in the anatomy textbooks, mainly because it is more difficult to study cerebral arteries anatomically in the corpse than radiologically in the living being. A simple diagram made by Fischer (fig. 1) indicates the main features and illustrates very clearly the importance of two views at right angles, lateral and antero-posterior. The main arteries, the internal carotid, anterior and middle cerebral, are indicated  $C_1, C_2, \dots; A_1, A_2, \dots; M_1, M_2, \dots$ , respectively. This facilitates orientation particularly near the bifurcation of the internal carotid artery. It will be noticed that the termination of this artery and the origins of the anterior and middle cerebral arteries form a "T" (see  $C_1, A_1$ , and  $M_1$  in fig. 1). This "T" shape is important in the diagnosis of vessel displacement. The posterior cerebral artery is not included in the diagram, but it is filled from the internal carotid artery in about one-third of cases so it is an important vessel in carotid angiography. Further anatomical details can be obtained from Moniz' works.

**Indications for carotid angiography.**—Some are clear cut, while the value of others depends upon judgment and experience. Vascular lesions of the brain must obviously be investigated primarily by angiography (see Table I, Groups A and B). The investigation of traumatic

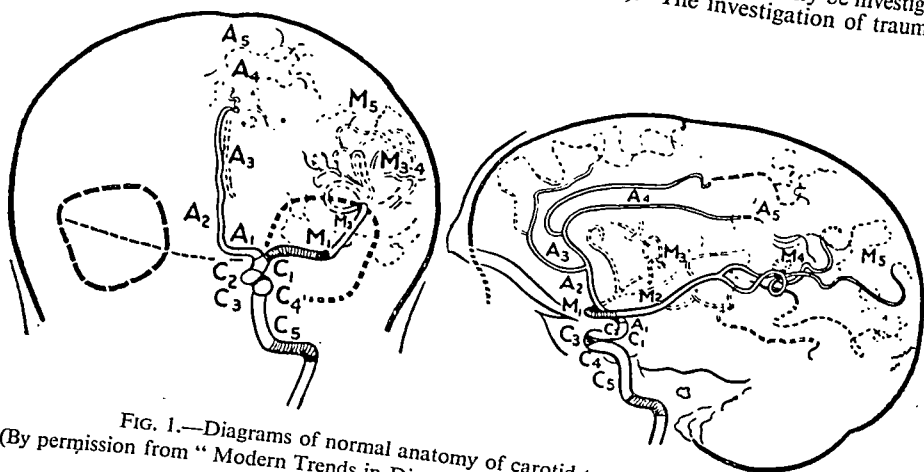


FIG. 1.—Diagrams of normal anatomy of carotid tree (after Fischer).  
(By permission from "Modern Trends in Diagnostic Radiology" by J. W. McLaren, London.)

conditions (Table I, Groups C and D) is still in its infancy. Many tumours can be diagnosed by angiography (Table I, E), but pneumo-encephalography is frequently a better method. As things stand at present pneumo-encephalography is the method of choice in investigating mid-brain and posterior fossa lesions.

**Subarachnoid hæmorrhage** (Group A) is nowadays a clear-cut indication for angiography in just the same way that intravenous pyelography is indicated in cases of hæmaturia. Aneurysms are the commonest cause of subarachnoid hæmorrhage. Sometimes they can be localized clinically, while on the other occasions there are no localizing signs and bilateral angiography may be necessary. Negative angiograms do not necessarily exclude an aneurysm, even if a vertebral angiography is also performed and good filling of the basilar artery and its branches is obtained. The explanation must be that some aneurysms do not fill with the contrast substance for some reason or another. The subject of aneurysms has been fully discussed by Jefferson in his writings in the *Proceedings* of this Society and elsewhere. (Jefferson, 1937, 1938, 1947.)



FIG. 2A.—Lateral arteriogram of large angioma. Note hypertrophied anterior cerebral artery and filling of straight sinus, all in the same phase—never seen in normal cases.

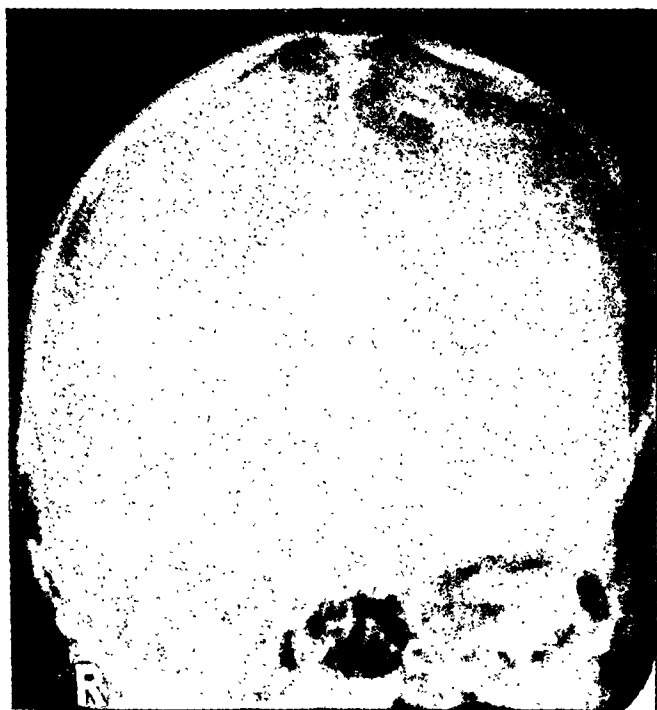


FIG. 2B.—Same case in frontal view.



FIG. 3.—Thrombosis and complete occlusion of internal carotid artery about 2 cm. from origin (†). This is one of the classical sites.

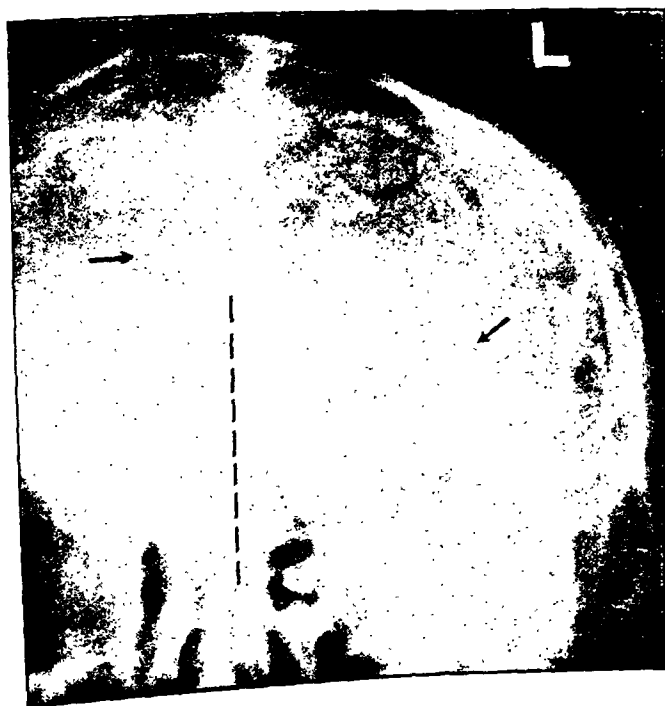


FIG. 4.—Subdural hæmatoma. Absence of vessels between inner table of skull and brain surface (2 arrows) and displacement of anterior cerebral artery across the mid-line (single arrow).

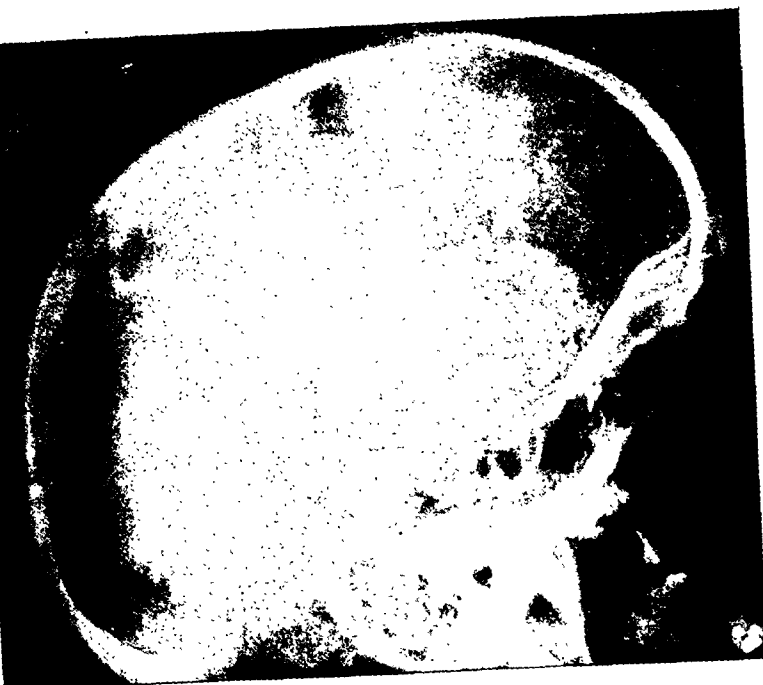


FIG. 5.—Pterion meningioma, full of contrast in venous phase ("blush"). Note that all the contrast substance has left the arteries and that convexity veins draining to the superior sagittal sinus are filled.



FIG. 6.—Frontal astrocytoma. Anterior cerebral artery and its proximal branches are all very stretched. Note absence of tumour vessels.

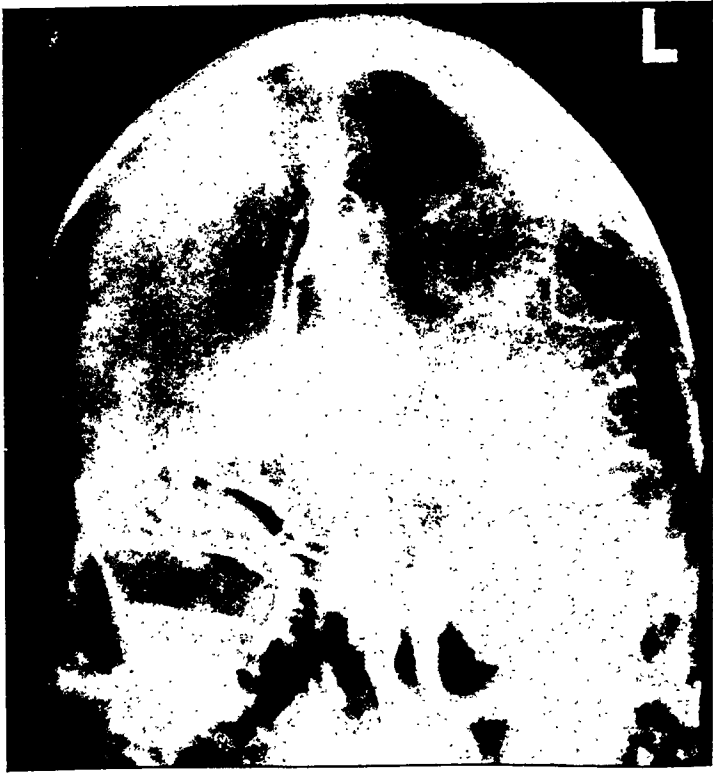


FIG. 7.—Same case as fig. 6. Anterior cerebral artery very stretched and pressed across the mid-line.



FIG. 8.—Coronal section to show astrocytoma: through frontal lobes of hardened brain of case illustrated in figs. 6 and 7.

NOTE.—Owing to limitations of space only very few of the illustrations shown at the reading of the paper can be reproduced.



Occasionally, instead of finding an aneurysm in a patient with a history of subarachnoid hæmorrhage, one discovers an angioma (syn. arteriovenous aneurysm). The following case is an example: J. R., a woman aged 31, gave a history of four attacks of generalized severe headache associated with neck stiffness and backache on one occasion. These attacks had occurred over a period of six years and lumbar puncture showed blood in the cerebrospinal fluid on each occasion. After the last attack she was admitted under the care of Mr. Wylie McKissock. Physical examination showed some inco-ordination of the left arm. A systolic bruit was audible over the closed eyes, more marked on the right. Angiography showed a large angioma in the mid-line, apparently drawing its blood supply from both anterior cerebral arteries (fig. 2, A and B). As is usual in these cases the blood flowed very rapidly through the angioma and contrast material was seen in the large venous sinuses even in the arterial phase. In a normal case the large venous sinuses do not fill for three or four seconds after the arterial picture is taken.

I have no experience of the angiographic appearances in a tumour which has hæmorrhaged (Group A, 3).

TABLE I.—CEREBRAL ANGIOGRAPHY

1. *Carotid.* Valuable method. Simple. Comparable to intravenous pyelography.
2. *Vertebral.* Limited use. Rather difficult to perform.

## INDICATIONS FOR CAROTID ANGIOGRAPHY: FIVE MAIN GROUPS

| A. Subarachnoid hæmorrhage                           |  | E. Intracranial expanding lesions. (Non-traumatic)              |      |       |          |           |
|------------------------------------------------------|--|-----------------------------------------------------------------|------|-------|----------|-----------|
| 1. Congenital aneurysms                              |  | 1. Certain aneurysms                                            |      |       |          |           |
| 2. Bleeding angioma                                  |  | 2. Angiomas which have not bled                                 |      |       |          |           |
| 3. Bleeding tumour                                   |  | 3. Meningiomas.                                                 |      |       |          |           |
|                                                      |  |                                                                 | Size | Shape | Position | Pathology |
|                                                      |  | 4. Malignant gliomas.                                           | "    | "     | "        | "         |
|                                                      |  | *5. Metastases.                                                 | "    | "     | "        | "         |
|                                                      |  | 6. Expanding lesion showing vessel displacement.                |      |       |          |           |
|                                                      |  | (a) One of above lesions failing to show characteristic pattern | "    | "     | "        | No        |
|                                                      |  | (b) Benign glioma (astrocytoma, oligodendroglioma)              |      |       |          |           |
|                                                      |  | (c) Abscess                                                     |      |       |          |           |
|                                                      |  | (d) Granuloma                                                   |      |       |          |           |
| B. Arterial occlusion                                |  |                                                                 |      |       |          |           |
| 1. Thrombosis                                        |  |                                                                 |      |       |          |           |
| 2. Embolism                                          |  |                                                                 |      |       |          |           |
| C. Cranio-cerebral injury                            |  |                                                                 |      |       |          |           |
| 1. Extradural hæmatoma                               |  |                                                                 |      |       |          |           |
| 2. Acute subdural hæmatoma                           |  |                                                                 |      |       |          |           |
| 3. Intracerebral hæmatoma                            |  |                                                                 |      |       |          |           |
| 4. Cerebral œdema                                    |  |                                                                 |      |       |          |           |
| D. Sequela of trauma                                 |  |                                                                 |      |       |          |           |
| 1. Subdural hæmatoma. Common                         |  |                                                                 |      |       |          |           |
| 2. Arteriovenous fistula at cavernous sinus. V. rare |  |                                                                 |      |       |          |           |

\*Certain if multiple.

*Carotid thrombosis* is not so rare as is generally supposed. Moniz says the possibility should be considered in any obscure case of hemiplegia. I have seen three cases in the last two years. There are two sites of election for the obstruction: (1) about one inch (2.5 cm.) distal to the bifurcation of the common carotid artery, and (2) adjacent to the anterior clinoid process where the internal carotid artery pierces the dura. The condition is often seen in younger people, unlike femoral arterial thrombosis which is usually seen in the late fifties or sixties.

An important point in the diagnosis is the necessity of showing enough of the neck on the radiograph so that the bifurcation of the carotid is seen, otherwise it can easily be assumed that the external carotid artery has been punctured, as it alone is seen on the radiograph. This difficulty may not be at all easy to overcome in short-necked individuals. Fig. 3 is an example of a thrombosis low in the neck, about one inch distal to the bifurcation of the common carotid artery. The patient was a woman aged 40.

I have only seen one case of embolus—a block at the origin of the middle cerebral artery.

Angiography has been little used in this country in cases of acute head injury (Table I, Group C), but Torkildsen (1946) claims to have found it useful.

*Chronic subdural hæmatoma* (Group D) gives a well-known pathognomonic appearance in a frontal arteriogram, but few cases reach the radiologist as the surgeon usually establishes the diagnosis with a burr hole. I have had only one such case. A frontal picture is essential for the diagnosis. The middle cerebral vessels are seen to be pressed inwards from the inner table of the skull (fig. 4).

*Arteriovenous fistula* at the cavernous sinus is a rare sequela to trauma and I have not had such a case.

## SPACE-OCCUPYING LESIONS

Many intracranial expanding lesions can be diagnosed by arteriography and sometimes more positive information is given than by pneumo-encephalography (Table I, Group E). Certain large aneurysms and angiomas are included in this group. Recently I saw a case, a woman aged 64, who had been seen by a very experienced neurologist. A diagnosis of olfactory groove meningioma was made and this appeared to be confirmed by ventriculography. The anterior horns of the lateral ventricles were pressed upwards in the characteristic manner. Exploration, however, revealed a large aneurysm of the anterior cerebral artery which was subsequently confirmed by arteriography.

## TUMOUR DIAGNOSIS

It is now well recognized that angiography is very valuable in tumour diagnosis, for certain tumours are sufficiently vascular to outline themselves with the contrast substance. Furthermore tumours of different types have different vascular patterns. Thus one is able to diagnose not only the size, shape and position of a tumour, but also its pathology. There are also a large number of intracranial expanding lesions with relatively poor blood supply, but nevertheless they manifest themselves angiographically by the vascular displacement they cause. In such cases one cannot make a positive pathological diagnosis.

Modern methods of ventriculography enable one in nearly all cases to localize a tumour accurately and to describe to some extent its size and shape. Rather rarely, however, is one in a position to describe the pathology. Other advantages provided by angiography are (1) that the investigation does not usually upset the patient or interfere with the intracranial hydrodynamics and so immediate operation is not necessary, as with ventriculography, and (2) it is often easier to puncture the appropriate carotid artery than the appropriate lateral ventricle. Not infrequently ventriculography only gives a filling of the contralateral ventricle, as the homolateral ventricle is too squeezed and displaced for puncture. In such cases one only sees a shift of the septum lucidum away from the affected side, and so one can give the surgeon no more information than he may have known clinically.

Generally speaking when a supratentorial tumour is suspected and can be lateralized fairly certainly clinically, or quite certainly by pineal shift, angiography should be undertaken before ventriculography. On the other hand unlateralized tumours are probably better investigated first by ventriculography as it is surely bad practice to perform "blind" angiographies, hoping that one is injecting the appropriate side.

With the object of trying to assess the relative merits of angiography and pneumo-encephalography in supratentorial tumour diagnosis, Wickbom (1948) analysed all the tumour cases on whom angiograms were performed at the Serafimer Hospital, Stockholm, between 1934 and 1946. He collected 376 tumour cases out of about 1,500 angiographic examinations. I have tried to abstract his findings in Table II (see p. 890), and certain conclusions can be briefly discussed. In spite of the small number of cases in some groups the figures were convincing. For example, eight out of eight subfrontal tumours could be positively diagnosed. This is a finding one would expect when one considers that the proximal portion of the anterior cerebral artery is so adjacent to the subfrontal region, and thus easily liable to changes in shape from pressure below by all but the smallest of tumours. On the other hand only 50% of parasagittal frontal tumours could be diagnosed (13 out of 24). Wickbom explains this by stating that the pericallosal artery is relatively fixed and not easily depressed, while sometimes tumours grow around it and so do not depress it. Nearly all parietal and occipital tumours could be localized angiographically and some showed tumour vessels indicating their pathology. The same applies to temporal lobe tumours, but it must be remembered that Lindgren's (1948) classical monograph on the temporal horn showed that pneumo-encephalography was an exceedingly accurate method of diagnosis and frequently differentiated between intracerebral and extracerebral lesions.

Central, deep-seated, and supra- and para-sellar lesions were not very satisfactorily diagnosed by angiography, but aneurysms must always be excluded when considering lesions around the sella.

The conclusion to be drawn is that angiography and pneumo-encephalography are complementary to one another and often both investigations are necessary before the surgeon is provided with adequate information.

## PATHOLOGY

A study of Table I, E shows how the pathology of certain tumours can be diagnosed angiographically.

(1) *Meningiomas*.—Many of these tumours fill with the contrast substance in the arterial phase and often there is a lag before the tumour empties, so that a so-called "blush" is seen in the phlebograms (fig. 5). I have seen this blush persist for as long as twelve seconds after injection of the contrast. (Normally all the contrast has left the brain in five seconds.) Unfortunately all meningiomas do not show a blush and very occasionally malignant gliomas

do. I have seen one such case. However, bearing this exception in mind, this sign is most valuable for the diagnosis of meningiomas.

(2) *Malignant gliomas*.—A large proportion of these tumours are known by pathologists to be very vascular and this feature is well shown angiographically. Classically one sees many small abnormal vessels having the appearance of minute arteriovenous aneurysms. These vessels are sometimes best seen on phlebograms and for this reason, if for no other, the taking of phlebograms is necessary in angiography. Different writers vary in their opinions as to the frequency of the presence of pathological vessels in malignant gliomas. This is probably partly due to the fact that only selected cases are submitted to angiography. Hemmingson (1939) found abnormal vessels in 23 out of 36 cases. When the characteristic pattern is seen it is very helpful to the surgeon and the patient may be saved a craniotomy. However, too much reliance should not be placed on the angiographic interpretation of the morbid histology, for certain meningiomas may simulate gliomas very closely angiographically as I have already mentioned. Therefore a biopsy is nearly always necessary to confirm the diagnosis.

(3) *Metastases*.—Certain metastases also show a characteristic angiographic pattern. Small arteriovenous aneurysms similar to those seen in malignant gliomas may be present. Usually the periphery of a metastatic tumour is better outlined than that of a glioma. If multiple tumours are seen on angiography the diagnosis is virtually certain, as multiple meningiomas and multiple gliomas are very rare indeed.

(4) *Avascular expanding lesions*.—Here the term "avascular" implies that contrast-filled vessels are not to be seen on the radiograph in the situation of the tumour. Table I, E, 6 lists these types. They manifest themselves by vessel displacement. This is sometimes very difficult to diagnose, and increasing accuracy only comes with experience and a knowledge of the limits of the normal vascular patterns. The variations of normal are quite considerable, but this adds very much to the fascination of angiographic interpretation.

Space does not permit any discussion of the classical vascular displacements produced by tumours in various situations, but the frontal astrocytoma, mentioned at the beginning of the paper, which came to autopsy, will serve as an example and the photograph of the sectioned brain provides final proof of the site of the tumour.

The patient was a man aged 27 who had suffered from epilepsy for six years. For the last nine months he had had headaches in the right temporal region. For six months he had had diplopia and for two weeks noises in the left temple. Examination revealed chronic papilloedema, left proptosis and ptosis and diplopia.

A left arteriogram was performed and, as already mentioned, coma supervened two and a half hours afterwards, and the patient died the following day. Nothing was found at autopsy referable to the arteriography, but Broman and Olsson (1948) have found in rabbits that 50% and 70% contrast material cause a breakdown of the blood-brain barrier. It seems likely that this happened here, though 42.5% was the strongest contrast used, and as a result the brain, which was perhaps already oedematous, became more so and caused so much herniation of the uncus as to be incompatible with life. Fig. 6 shows the stretching of the anterior cerebral artery and its branches and a backward displacement of the anterior loop of the pericallosal artery. Fig. 7 shows the lateral displacement of the anterior cerebral artery and fig. 8 shows the tumour at autopsy.

#### SUMMARY

I must again stress the great importance of two right-angled views in nearly all angiographic studies. So often in the literature one finds that only lateral projections are taken.

One of the most important problems is to decide when angiography, pneumo-encephalography or both are necessary in neurological diagnosis. There are certain clear-cut indications for each of them—angiography for vascular lesions of all kinds and pneumography for posterior fossa lesions. A rough rule for the investigation of supratentorial expanding lesions is that tumours near vessels show better by angiography and those near the ventricles by pneumo-encephalography. There are some exceptions to this rule, notably that the pericallosal artery is fairly fixed and is resistant to pressure; also a few tumours grow around the vessel without displacing it. Let us remember that normal ventricles are much more constant in size and shape than normal arteries, which show considerable variations and can mislead the most experienced observers. The slightest displacement of the ventricular system may enable accurate localization to be made: such as half a centimetre shift of the temporal horn. The same cannot be said of the arteries. However, even when arteries are not displaced an exact diagnosis can be made if tumour vessels are filled. Further, if vessels are stretched but not displaced, the abnormality can be diagnosed as one's experience grows. Thus it is obvious that the two methods are complementary to one another. Generally speaking if straight X-rays or clinical or electro-encephalographic signs lateralize a tumour,

arteriography should be undertaken first. In my view another important point is that one should avoid upsetting the intracranial hydrodynamics when they are known to be abnormal (ophthalmoscopy and straight X-rays tell us this) and lumbar puncture can be very dangerous in this respect, while angiography is usually not so.

Blind bilateral angiography, except for an unlocalizable source of subarachnoid hæmorrhage and occasional other cases, is not good practice. Now that practically no tube or even solid organ of the human body is immune from the assault of radiologists it behoves us to be doubly careful in using our weapons intelligently. We should try to avoid firing all our big guns in a blind salvo at once, but use them strategically and seek to obtain the maximum effect with the minimum expenditure of ammunition.

TABLE II.—376 CASES 1934-1946  
(Abstracted from I. Wickbom's monograph "Angiography of the Carotid Artery")

|                                             | Cases | Positive                                                                                                                 | Tumour vessels | Doubtfuls and negative | % positive | Vessel displacement                                                                     |
|---------------------------------------------|-------|--------------------------------------------------------------------------------------------------------------------------|----------------|------------------------|------------|-----------------------------------------------------------------------------------------|
| <b>GROUP 1</b>                              |       |                                                                                                                          |                |                        |            |                                                                                         |
| <i>Frontal</i>                              |       |                                                                                                                          |                |                        |            |                                                                                         |
| (a) Subfrontal                              | 8     | 8                                                                                                                        | 1              | 0                      | 100        | (a) Ant. cerebral artery elevated                                                       |
| (b) Parasagittal                            | 24    | 13                                                                                                                       | 5              | 11                     | 50         | (b) Pericallosal artery depressed                                                       |
| (c) Low lateral                             | 41    | 35                                                                                                                       | 23             | 6                      | 85         | (c) Ant. sylvian arteries depressed                                                     |
| (d) Convexity                               | 33    | 23                                                                                                                       | 13             | 10                     | 70         | (d) Half-way between (b) and (c)                                                        |
| (e) Deep (infiltrating and corpus callosum) | 20    | 12                                                                                                                       | 9              | 8                      | 60         | (e) Not describable in few words                                                        |
| <b>GROUP 2</b>                              |       |                                                                                                                          |                |                        |            |                                                                                         |
| <i>Parietal</i>                             |       |                                                                                                                          |                |                        |            |                                                                                         |
| (a) Parasagittal                            | 18    | 16                                                                                                                       | 3              | 2                      | 90         | (a) Pericallosal artery depressed                                                       |
| (b) Antero-superior                         | 40    | 35                                                                                                                       | 7              | 5                      | 87         | (b) Sylvian arteries depressed                                                          |
| (c) In or below sylvian fissure             | 24    | 24                                                                                                                       | 12             | 0                      | 100        | (c) Spreading of sylvian arteries                                                       |
| <b>GROUP 3</b>                              |       |                                                                                                                          |                |                        |            |                                                                                         |
| <i>Occipital</i>                            | 14    | 13                                                                                                                       | 8              | 1                      | 92         | Forward displacement of terminal sylvian arteries                                       |
| <b>GROUP 4</b>                              |       |                                                                                                                          |                |                        |            |                                                                                         |
| <i>Temporal</i>                             |       |                                                                                                                          |                |                        |            |                                                                                         |
| (a) Anterior                                | 86    | 83                                                                                                                       | 32             | 3                      | 96         | (a) Elevation of anterior sylvian arteries. Elevation of M <sub>1</sub> in frontal view |
| (b) Posterior                               | 21    | 20                                                                                                                       | 11             | 1                      | 95         | (b) Sylvian arteries elevated                                                           |
| (c) In sylvian fissure                      | 7     | 7                                                                                                                        | 3              | 0                      | 100        | (c) Merges into Parietal (c)                                                            |
| <b>GROUP 5</b>                              |       |                                                                                                                          |                |                        |            |                                                                                         |
| <i>Central</i>                              | 22    | No pathognomonic vascular displacement. 5 cases showed tumour vessels indicating localization and pathology              |                |                        |            |                                                                                         |
| <b>GROUP 6</b>                              |       |                                                                                                                          |                |                        |            |                                                                                         |
| <i>Supra- and para-sellar</i>               | 9     | Features (1) Widening of carotid siphon<br>(2) Elevation of A <sub>1</sub> in frontal view<br>Useful to exclude aneurysm |                |                        |            |                                                                                         |

#### BIBLIOGRAPHY

- BROMAN, T., and OLSSON, O. (1948) *Acta Radiol.*, 30, 326.  
 HEMMINGSON, H. (1939) *Acta Radiol.*, 20, 499.  
 JEFFERSON, G. (1937) *Brain*, 60, 444.  
 — (1938) *Brit. J. Surg.*, 26, 267.  
 — (1947) *Proc. R. Soc. Med.*, 40, 419.  
 LINDGREN, E. (1947) *Brit. J. Radiol.*, 20, 326.  
 — (1948) *Acta Radiol. Suppl.*, 69.  
 LOMAN, J., and MYERSON, A. (1936) *Amer. J. Roentgenol.*, 35, 188.  
 TORKILDSEN, A. (1946) *Tidsskr. norske Laegeforen.*, 11, 1.  
 TURNBULL, F. (1939) *Amer. J. Roentgenol.*, 41, 166.  
 WICKBOM, I. (1948) *Acta Radiol. Suppl.*, 72.

Mr. J. Bryant Curtis, Professor Brodie Hughes, Mr. D. W. C. Northfield, Mr. Walpole Lewin and Dr. B. N. Klukvin took part in the subsequent discussion.

## Section of Psychiatry

President—J. R. REES, C.B.E., M.A., M.D., F.R.C.P., D.P.H.

[April 12, 1949]

### Clinical and Electroencephalographic Studies of Temporal Lobe Function

By J. H. REY, M.D., D. A. POND, M.R.C.P., D.P.M., and C. C. EVANS, L.R.C.P.,  
M.R.C.S.

#### INTRODUCTION

INTEREST in the relationship of temporal lobe dysfunction and mental disturbance has attracted the attention of an increasing number of workers. The literature on the subject has been summarized by Frantz (1947). Confusional states, dreamy states, hallucinations (visual, auditory, gustatory and olfactory) and amnesias have been reported by a great number of writers. Personality changes, which in the past have been neglected perhaps because of interest being focused on the frontal lobes, have lately attracted the attention of several workers. Experimental work, such as the classical studies of Klüver and Bucy (1939), has demonstrated that marked changes in behaviour follow bilateral excision of the temporal lobes in monkeys. Attempts at temporal lobotomy have been made by Obrador (1947) on patients with mental symptoms. With regard to the EEG it is well known that abnormalities are more frequently found in psychiatric cases than in control groups of normals. In 1942 Hill and Watterson, and later Hill (1944), reported on a group of aggressive psychopaths where EEG abnormality was located to the temporal areas.

The original impulse for this study came from one of us having had patients who had mental symptoms accompanying temporal lobe lesions and later patients with similar symptoms but only EEG evidence of temporal lobe disturbance. These observations, therefore, led us to collect cases of temporal lobe disturbance as judged by EEG criteria and to investigate possible clinical correlations. During the course of investigation it became clear the actual area with which we are probably concerned is at the posterior end of the temporal lobe, not the main body of it—that portion which merges into the adjacent parts of the parietal and occipital areas.

For this investigation about 3,000 EEG reports from the Maudsley Hospital have been examined, from which altogether 82 cases were chosen. The records were taken in the first place on a three-channel Grass electroencephalograph with standard electrode placements, as shown in fig. 1. In the majority of cases the abnormal activity was localized

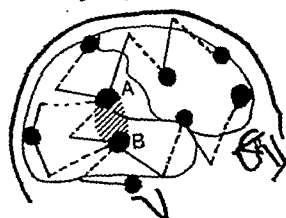


FIG. 1.—Diagram showing electrode positions A and B at which maximal abnormality or phase reversal occurs.

to the posterior and inferior positions as shown and the mastoid lead was used to demonstrate phase reversal with disturbances far down in the temporal lobe. Nearly all the subjects had more than one record, some half a dozen or more, and we have been able to re-examine more recently patients seen some years previously on a 6-channel apparatus with a view to more precise localization. The criteria of localization were: (1) Focal

localization by phase reversal of abnormal waves such as spikes, slow activity, &c. (2) Abnormal activity confined exclusively or predominantly to one side of the brain and occurring in one channel only.

There is general agreement among electroencephalographers that localization by phase reversal in the bipolar electrode technique is evidence that the activity is beneath the electrode at which such phase-reversal occurs. Activity confined to one channel, that is, seen only between two electrodes, is less certainly localized, although it is still in all probability cortical in origin. In some records abnormal activity is present on both sides and the rhythms are closely similar to the common bilaterally synchronous 4-7 c/sec. activity seen in about 10% of normal subjects and a variety of psychiatric conditions. Such rhythms though produced by cortical cells are commonly regarded as being paced by the thalamus or diencephalon. It is possible therefore for the abnormality responsible for bilaterally synchronous rhythm to be basal or cortical. In the cases here reported there was asymmetry of frequency, amplitude and per cent time of the abnormality so that it has been concluded that this asymmetry argues strongly for a cortical origin of the abnormalities.

Of the 82 cases of localized temporal abnormality, 23 were considered to be due to an acquired lesion, e.g. trauma, tumour, atrophy, &c.—on the basis of history, physical examination and post-mortem in some cases. 59 cases were considered to be of constitutional origin, i.e. not due to any acquired condition so far as could be ascertained by most careful study. The EEG's of the cases with acquired lesion were not further examined for peculiarities other than their localization, as this study is not primarily concerned with such cases.

#### CLASSIFICATION

An attempt was then made to classify the non-acquired cases from both the EEG and the clinical points of view independently of each other. The EEGs of the non-acquired cases were then examined for the actual type.

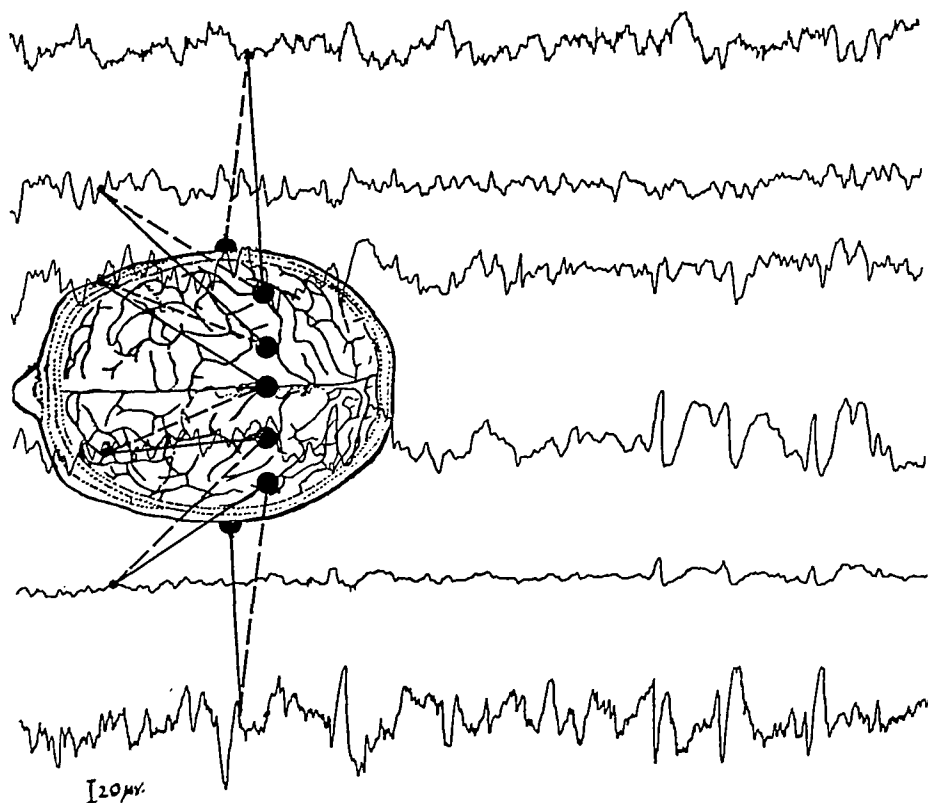


FIG. 2.—EEG, showing epileptic focus in the left temporal area (between channels 4 and 6), the electrodes being placed in a line from right to left mastoid.

A. *EEG classification*.—It was found that the EEG records could be classified into three main groups:

(1) *The epileptic records*: These show typical epileptic features. They comprise cases whose records show undoubted epileptic foci—either spike foci or slow wave foci with other epileptic features in the record (fig. 2). These foci are not present in every record, but when present are always in the same place. There are also five other records which show no true focus by phase reversal, but show spike activity maximal in the temporal area.

(2) *The epileptoid records*: There are 13 records which do not contain such specific findings as the epileptic ones but have paroxysmal sharp waves, paroxysmal fast and slow activity (e.g. fig. 3) or runs of fast beta activity as well as the theta disturbances localized

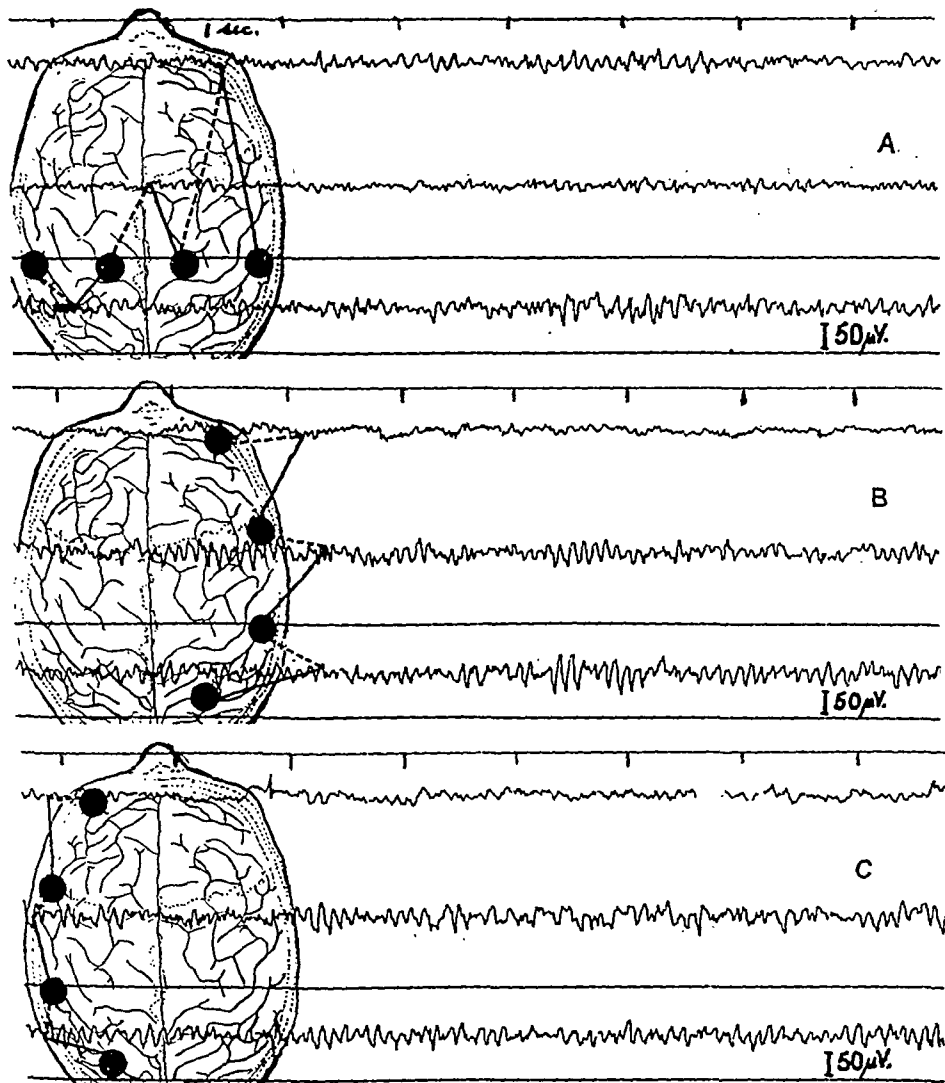


FIG. 3.—Three sections of EEG from the same patient showing localization of fast and slow dysrhythmia ("epileptoid") to the left temporal area in transverse (A) and anterior-posterior (C) recording.

in the temporal areas. Such records are well known to occur commonly in epilepsy but are also seen occasionally in schizophrenia and psychopathic states. These records we have called epileptoid.

(3) *The constitutional records*: The third group of records consists of those in which there is a slow wave dysrhythmia only, and none of the above described features. Five of these cases show delta rhythm (less than 4 c/sec.) foci by phase reversal (fig. 4) and twenty showed delta or theta dysrhythmias confined to the temporal regions and showing significant asymmetry of frequency and/or amplitude (fig. 5). These we have called the constitutional type of record.

B. *Clinical classification*.—A clinical study of these cases was made. All the patients had been previously examined by various psychiatrists both at the Maudsley and in some cases by outside psychiatrists as well. We have personally interviewed about 70% of these patients.

The cases were divided into two groups: the one with known acquired lesions such as tumour, trauma, infection, &c., and the other consisting of cases suffering from a "functional" type of illness in whom all of an acquired cerebral pathology had been eliminated, as far as possible.

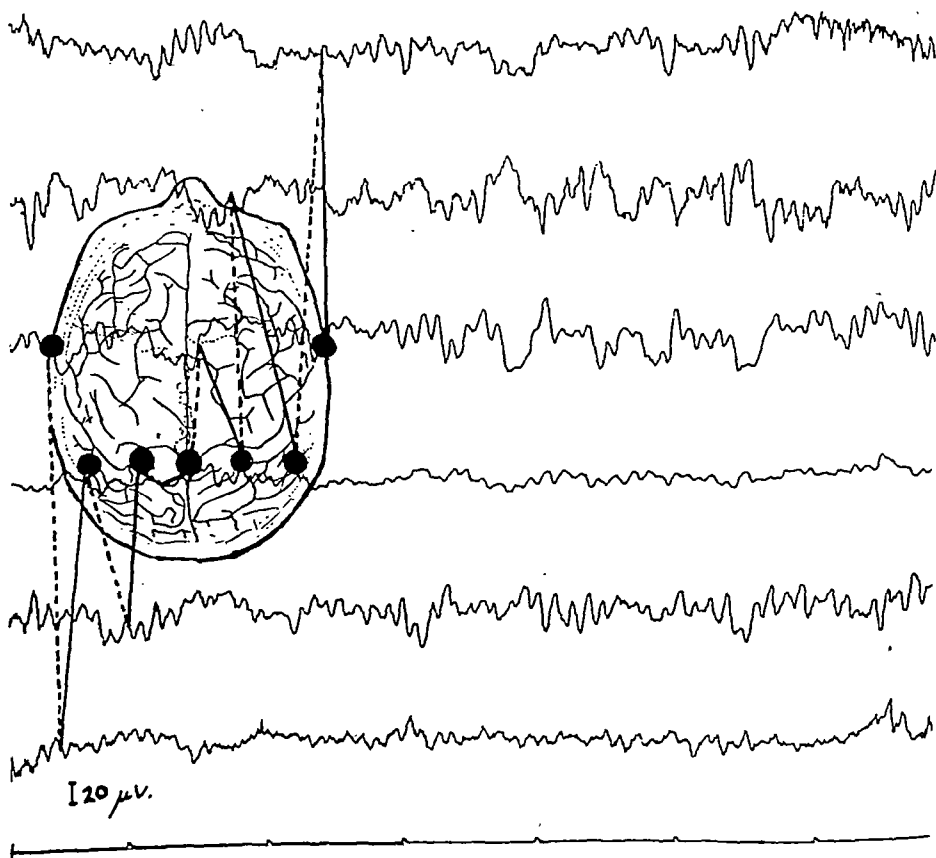


FIG. 4.—EEG showing slow wave ("constitutional") focus in the right posterior temporal area (between channels 2 and 3), the electrodes being placed in a posterior line from mastoid to mastoid.

These two groups will be described separately and we will first deal with the non-acquired or "functional" group. It was found that the patients from this group had certain psychopathological features in common which will be described. However, they also differed in certain aspects and these cases could be separated into two groups: those with and those without typical epileptic manifestations. The group without obvious epileptic manifestations could itself be subdivided into two sub-groups, the one being distinguished from the other by what might, for want of a better term, be called disorders of consciousness and behaviour of an episodic nature.

When the three clinical groups just described were compared with the EEG findings



they were found to correspond roughly to the three EEG types respectively and it was then decided to group the cases according to the type of EEG so that such classification would then have the advantage of being less dependent on individual assessment and thus be more objective.

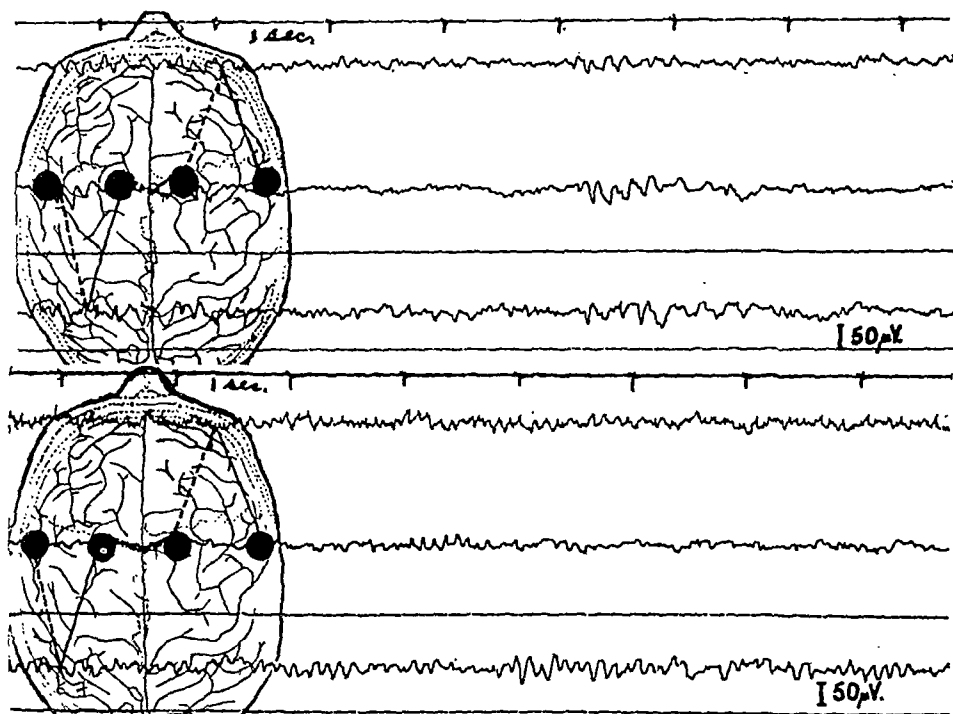


FIG. 5.—Records from different patients showing asymmetrical non-focal slow ("constitutional") dysrhythmia in the temporal regions.

#### PART I.—NON-ACQUIRED (FUNCTIONAL) CASES

##### A. CLINICAL FEATURES COMMON TO THE NON-ACQUIRED CASES.

As previously mentioned some features were found to be common to all cases to a fairly characteristic degree. They were:

(a) *Personality*: The personality of these patients is characterized by an inability to adapt themselves to their environment, by an inability to make friends or, if they do, to keep them; they cannot mix with other human beings in a normal way; they seldom keep to the same occupation, are hardly ever successful in whatever they attempt to do; they cannot face responsibility. Often they seem to be dependent on the stimulus of the moment. They have a tendency to live in fantasy more than reality. Certain words often recur in their description, such as "shy, bad mixer, no friends, cannot make friends, immature, ego-centric, nervous, irritable, sensitive, over-attached to family, did not play games", and so on.

Out of the 59 cases 40 showed this characteristic personality picture and in the other 19 cases the personality disturbance was not so marked.

A few examples from the personality assessment of these patients by the various psychiatrists in charge of the cases will illustrate this.

A boy of 14 is described as "a passive, dependent individual with impulsiveness, some short-lived temper-tantrums, a rich fantasy life and probably undifferentiated sexuality. He has poor concentration, is a cry-baby, stubborn and shows some manifestations of chronic emotional disturbances. At home he does things just to annoy his parents".

A boy of 11 "is an extreme of personality type with gross disturbance of behaviour, paranoid characterology, impossible to maintain contact with him. Always he was a sorry, lonely figure with no friends, unreliable and untrustworthy".

A girl of 13 is described as "very immature, like a child of 2. Her interest is centred on food. The members of the family are perfectly horrible if they do not do as she wants. Difficult behaviour at home, hysterical, screaming and quarrelling. Twelve different billets during evacuation".

(3) *The constitutional records*: The third group of records consists of those in which there is a slow wave dysrhythmia only, and none of the above described features. Five of these cases show delta rhythm (less than 4 c/sec.) foci by phase reversal (fig. 4) and twenty showed delta or theta dysrhythmias confined to the temporal regions and showing significant asymmetry of frequency and/or amplitude (fig. 5). These we have called the constitutional type of record.

B. *Clinical classification*.—A clinical study of these cases was made. All the patients had been previously examined by various psychiatrists both at the Maudsley and in some cases by outside psychiatrists as well. We have personally interviewed about 70% of these patients.

The cases were divided into two groups: the one with known acquired lesions such as tumour, trauma, infection, &c., and the other consisting of cases suffering from a "functional" type of illness in whom all of an acquired cerebral pathology had been eliminated, as far as possible.

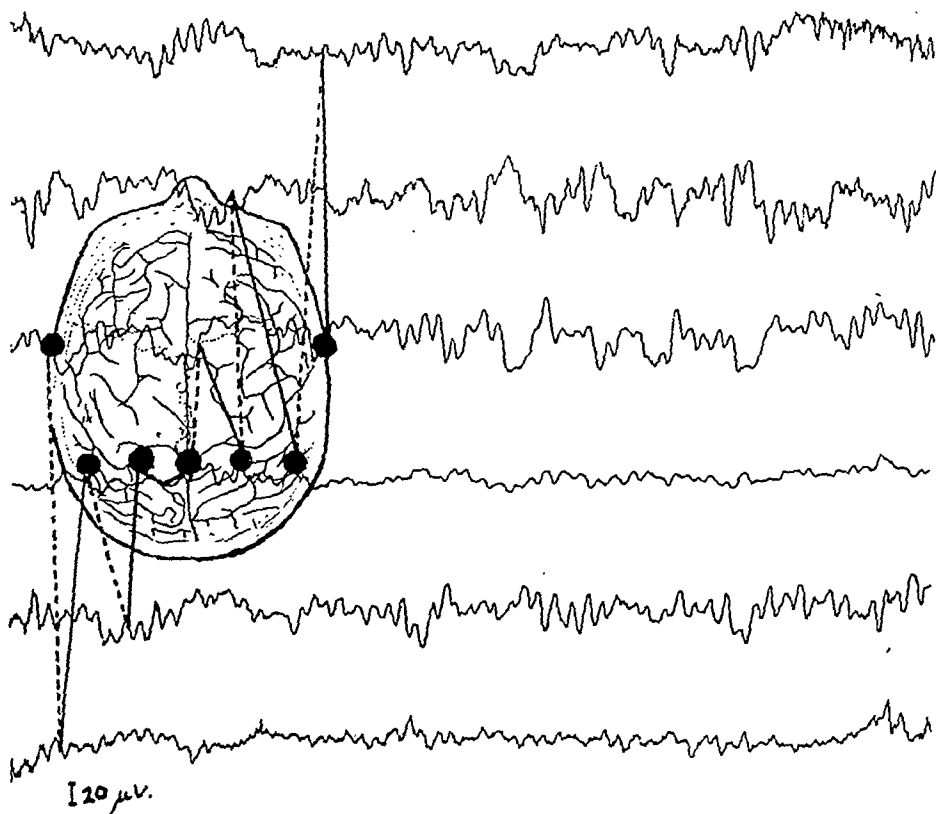


FIG. 4.—EEG showing slow wave ("constitutional") focus in the right posterior temporal area (between channels 2 and 3), the electrodes being placed in a posterior line from mastoid to mastoid.

These two groups will be described separately and we will first deal with the non-acquired or "functional" group. It was found that the patients from this group had certain psychopathological features in common which will be described. However, they also differed in certain aspects and these cases could be separated into two groups: those with and those without typical epileptic manifestations. The group without obvious epileptic manifestations could itself be subdivided into two sub-groups, the one being distinguished from the other by what might, for want of a better term, be called disorders of consciousness and behaviour of an episodic nature.

When the three clinical groups just described were compared with the EEG findings

One case who went from doctor to doctor and hospital to hospital has been variedly called, "Obsessional personality, schizoid personality, depersonalization syndrome, anxiety neurosis and hysteria".

A woman of 38 was diagnosed as follows: "Hysterical personality with paranoid symptoms likely to end up as a chronic, possibly mildly adjusted schizophrenic." In a previous hospital she had been diagnosed as "Psychopathic personality with paranoid, hysterical and aggressive outbursts".

Though the diagnosis of schizophrenia was only made once, and in a catatonic patient, reference to a "schizophrenic impression" is made 14 times somewhere in the description of these patients, and reference to hysteria is made 19 times.

Though on first impression it seems that diagnosis was varied and inconsistent in these cases, in fact, it was remarkably consistent. Three factors seem to be always present: the lack of contact with the environment which called for the schizophrenic impression, the aggression and inadequacy which called for the psychopathic impression and the childishness and hysteriform attacks which called for the hysterical impression.

(e) *Family history*: In 32 of these cases there was a family history of mental abnormality. The abnormalities recorded included neurosis, psychosis, psychopathic traits and alcoholism.

A history of clinical epilepsy was only present in the epileptic group, in 3 cases. No cases of epilepsy were recorded in the epileptoid or constitutional groups.

(f) *Physical examination*: Although all the cases had had a physical examination, we re-examined 26 of them neurologically to find out any minor constitutional defects such as differences in their reflexes when both sides of the body were compared, motor inco-ordination, and so on.

In only 2 cases was the result of the examination quite normal.

Nearly everyone of these cases showed a greater or lesser degree of inco-ordination of movement as well as spread of activity to neighbouring groups of muscles and sometimes to the whole body.

One-sided facial weakness was present in a striking way in 8 patients. In 5 cases it was on the right and in 3 on the left. This defect was of the upper motor neurone type and sometimes was best observed when watching the patient speak. In 2 cases this was, indeed, very striking for the patient appeared to be talking with only one side of his face.

The majority of cases showed differences in their reflexes between the right and the left sides. The left side was found to be brisker than the right more often than the reverse. Areflexia was present in 2 cases. Differences of muscular tone were also observed. There was a difference in the reflex of Babinski when both sides were compared and in 6 cases there was a definitely equivocal response. In 4 cases this was found on the right side and on the left in 2 cases.

(g) *Somatotyping*: An assessment of these patients' somatotype was attempted. No actual measurements were done as our idea was only to obtain a rough estimate of the physique in our group of cases in order to know if any type predominated. The Kretschmerian classification was used. It was found that asthenic traits appeared 19 times, hypoplastic 17 times, athletic 11 times, dysplastic 9 times and pyknic once. It is thus clear, however rough was the assessment, that our group tends to be found towards the asthenic end of the Kretschmerian scale.

(h) *Personality tests*: A number of tests were given to these patients in order to obtain an assessment of personality independent of the psychiatrist's opinion. A self-rating questionnaire with 100 items and the word-association list for neuroticism was given by Dr. Lovett Doust to a random sample of 24 patients from our group of cases. The Rorschach test could only be given to 12 cases.

On analysis of the patient's answers, it was found that they formed a fairly homogeneous group in so far as the high incidence of certain traits was thus brought to light.

Outstanding characteristics were the incidence of: poor interpersonal relationship, of a failure in achieving a reality principle as is shown by their indulging freely in a world of phantasy, and using phantasy as a favourite method of solving their difficulties; they were markedly over-dependent, regretted their childhood, were insecure and needed protection; even in a self-rating questionnaire they admitted to impulsiveness, tempers and aggressive feelings, sexual immaturity was frequent as shown by various sexual fears and phantasies, by their attitude to marriage, and physiologically by delayed menarche, dysmenorrhoea, &c. . . . They had numerous childish fears and phobias, they showed distractibility as well. 13 cases had experienced unusual or strange body sensations.

#### B. CLINICAL CORRELATES OF EEG TYPES.

(a) The constitutional cases show no other conspicuous clinical features than those recorded as common to all groups. Mild amnesic phenomena were present in 5 cases.

(b) The epileptoid group, apart from showing the characteristics common to all three groups, presented disturbances of consciousness and behaviour of an episodic nature.

A young man of 20 is described as having been in pre-school days very small and very shy, then a poor scholar, lazy and unhappy when away from mother. He epitomizes his attitude in the following words "I mustn't let work interfere with pleasure".

A woman of 27 is described as self-centred, selfish, hypochondriacal, over-critical, ambivalent, irritable. This woman's main trouble was her incapability of dealing with her married life, both from the sexual side and the responsibilities of home. She bitterly regretted her home, her parents, and her childhood days. In the course of attempted therapy she said, "I know I am not grown up, I know I cannot face responsibility but then I have never wanted to grow up, I have always wanted to be a Peter Pan; I know I cannot change". Taken through the Children's Department by a doctor, she asked about the place and was told it was the Children's Department. "Oh!" she said, "but this is where I belong."

(b) *Aggression and irritability*: Aggression of a pathological degree and of an overt type was present in 29 cases and irritability was present in another 15, that is, in 44 out of 59 cases. Here are some examples taken at random:

A boy of 17 is described as aggressive and boastful, he provokes other children and gets bitten by them, he gets into attacks of rage and says that he does not remember afterwards.

A woman of 38 cannot keep any employment, is resentful, irritable, restless, generally aggressive, and has crying and aggressive outbursts during which she throws things about.

Some cases are more violent than others; thus, a boy of 15 is described as very aggressive and sadistic. "He hits his grandmother, beats his half-brother, whom he ties down to do so. He uses intimidation and threats to obtain money. He is often insolent."

A woman of 31 is described by her husband. He lives in continual terror of her. In her rages she would attack him with knives and had even attacked the baby. "If I had not been in time the child would not have been alive to-day." She had smashed all the windows and part of the furniture.

Finally, the description of the personality of a boy of 16 is given by a probation officer. "On probation for breaking in and larceny and setting the place where he works on fire. Is very hot tempered, but intelligent. Is only a twelve pounder, tries to fire 16 inch shells. Might make a good trade union leader."

(c) *Anxiety*: The anxiety shown by these patients appeared to be different from the anxiety of the ordinary psychoneurotic and its accompanying degree of introversion and rationalization. It seems to be a sensation at a much lower level of experience, something less psychic, expressed in the body as well as in the mind, something that wants to break out all the time. It is also probably mixed with tension and the sense of an impending something that is going to happen any moment.

This is a general emotional state which can be observed with its varying degree of exacerbation. The patient does not always complain of that state but lives it instead. The word anger, we think, might be better perhaps than anxiety to describe this feeling. It is remarkable that in the epileptic group this feeling was sometimes present either as the attack itself or as an aura to a fit. We must say most emphatically that it was not only the apprehension of the fit by any means but a very different feeling of irresistible, intense, anxiety that swept away everything else. Here is an example of this type of prodromal anxiety:

"A woman of 37 had her first attack at the age of 28 when sitting in a cinema; she felt suddenly breathless, a feeling of fear came on her, she had never experienced anything like this before. She went out for some air, her heart started thumping, she jumped up with fright, she felt she was going to die, she felt she could not sit down, she could not talk to anybody. She just cannot tell how long the attack lasted."

"A man of 32 whose first attack came at the age of 26. He felt a gripping feeling round his heart, a feeling of fear came on him. He was fully conscious. Something was going to happen to him, but he did not know what. This was followed by a feeling of numbness in his left side. The anxiety caused by these attacks became so great that he attempted suicide."

In these two cases an attempt was made to demonstrate this particular anxiety occurring in attacks and which represents a sort of exacerbation of the more diffuse, more chronic and less intense anxiety, but similar in quality, found in these patients and present, as if to say, in the background.

(d) *Diagnosis*: The study of the diagnostic difficulties throws light on the problem these patients create if one attempts to place them in any of the accepted diagnostic classifications, even if psychopathy is included.

In the lower age-group the problem has been solved by labelling them "Behaviour Problem". The real problem, of course, remains, of how to define this term and what types of patients are included in it. This diagnosis applies to all cases throughout the three EEG groups in the lower age level.

In the older age-group in most cases the diagnosis is replaced by a short diagnostic formulation. This is not due to a general attitude to diagnosis, but definitely caused by difficulties of placing them into one category instead of another. Thus one experienced psychiatrist wrote: "? hysteria, ?? schizophrenia. A difficult problem because I find him inaccessible to a conventional approach."

have been grouped together (with the exception of the 5 cases showing runs of beta activity only) under the heading "Epilepsy".

When the scores on the verbal and performance scales are compared in each group it is found that in the Constitutional group the verbal scores tend to be higher than the performance scores, whilst in the Epileptic group the reverse tendency is observed. The 5 cases showing runs of beta activity as the only other abnormality present, apart from the non-paroxysmal slow activity (i.e. no paroxysmal slow and fast activity, sharp waves or spikes), behave as the Constitutional group. The possible meaning of these findings will be discussed later.

#### PART II.—ACQUIRED CASES

23 cases of acquired lesion of the temporal lobe were collected. Of these 6 were tumours and another 2 are under investigation and thought to be tumours. 5 are post-traumatic cases, 1 is an encephalitic, 1 is a case of eclampsia, 5 are cases diagnosed as cortical atrophy of doubtful origin. Of the tumours 6 out of 8 were on the right side, 1 was bilateral and 1 on the left. Of the traumatic cases, 1 was on the right (a depressed fracture) and 4 were on the left (no localized fracture), the 5 cases diagnosed as cortical atrophy of unknown origin are all left-sided abnormalities. 5 of the tumour cases were verified at operation or post-mortem.

*Symptomatology.*—These cases were admitted to the Maudsley because they were suffering from mental symptoms. The main features are summarized as follows:

(1) In all cases there were gross personality changes. These patients became less sociable, irritable and in some cases quarrelsome. Their capacity for work became impaired. Often their behaviour was described as hysterical; 2 cases were actually diagnosed as hysteria; in 3 cases a definite schizophrenic impression was produced.

(2) Hallucinations, auditory and visual, were present in 7 cases.

(3) Amnesia, memory defect and disorientation were present in some cases.

(4) Epileptic equivalent includes feeling of *déjà vu*, visions of past events, sensation of elation, or ecstasy, and also major and minor fits.

(5) In 2 cases the patients episodically experienced the sensation that somebody was standing behind them. This is a symptom that we have observed three times and which we would like to relate to a disorder of the body image.

We have found similarity in many ways between the symptomatology of the cases with acquired lesions of the temporal lobe and those cases selected on the basis of the presence of an EEG abnormality in the same area with no known acquired lesion. Here are two examples:

A woman of 60 is described as having been "always cheerful, sociable, fond of company and outdoor activity, busy with her home and visiting friends. At the age of 58 she started having turns in which she would suddenly go pale, stop talking and then make queer irrelevant remarks. She became very irritable and querulous and ill-tempered, unsociable and unfriendly and lost interest in her social activities. Her memory showed marked deterioration and she tended to become careless in her clothes and appearance." She was fully investigated and the diagnosis of Alzheimer's disease made. At post-mortem a well-encapsulated meningioma pressing on the left posterior inferior part of the temporal lobe was found.

A man of 32 was admitted complaining of headache and loss of power of concentration. There had been nothing in his past history except for some possible mild psychopathic personality traits. In the hospital his behaviour was grossly hysterical and very dramatic. His gait was unstable when in front of people; during a medical conference he addressed the doctors in a very histrionic way with dramatic affirmation that he was not putting up a show. His memory was bad only for some events that had got him into trouble in the Air Force, but when pressed he could remember them fairly well. He made approximate answers to questions in a way which was reminiscent of a Ganser state. Every investigation on this case remained negative. He died in the ward and he had a diffuse glioma on the right side which involved the right temporal lobe and extended to the ventricles.

#### PART III.—INTERRELATIONSHIP OF FACTORS OF SEX, EEG TYPES AND LATERALITY OF EEG ABNORMALITY

The group of 59 cases of "non-acquired" cases were examined statistically for any possible correlations between sex, EEG types and laterality of EEG abnormality (Table II).

For the sake of statistical analysis the epileptoid and epileptic EEG types were grouped together under the common heading of epilepsy. This group therefore consists of all those records which showed activity of a paroxysmal nature (i.e. paroxysmal fast and slow waves, sharp waves and spikes). The constitutional group has been described previously.

Several statistically significant correlations were arrived at which can be summarized as follows:

(a) Irrespective of the type of EEG abnormality there is a higher percentage of right-sided abnormality in males than females.

These were of two types. 9 patients of this group had attacks described as blackouts, fainting attacks, staring attacks, or blank periods. Here is a description of some of these "attacks":

A girl of 21 immediately after hearing of the death of a friend had an attack when she swayed, fell down, did not lose consciousness and cried afterwards. Since, she has been having repeated attacks where, without a warning, she suddenly falls or collapses, lies on the ground as if semiconscious, and flat on her back; she is of a good colour, her breathing is normal, her eyes shut and there are no movements. She comes round after two or three minutes.

A young man of 19 started having attacks of fainting followed by banging of the heart. These attacks were sometimes preceded by vertigo. They sometimes last for half an hour. He faints in the act of sitting or lying down so he now eats standing.

More dramatic is the occurrence in these patients of a particular type of "fit" which we will try to describe.

A young man aged 19 had attacks beginning with a feeling of fainting and dizziness. He then felt his legs become very weak, his face flushed, he started waving his arms and rushing about, asked for tablets, then rushed to the tap and put his head under the water. There was no loss of consciousness, no falling. The psychiatrist who saw the attack concluded "obviously functional".

A youth of 21, who suffered from recurrent periods of amnesia following traumatic war experiences, would lose his memory for periods of forty minutes, during which time he had fallen on to the ground, struggled, shouted and sworn and had required to be held down.

In spite of the EEG findings, which were only of an epileptoid nature, none of these cases was considered clinically to be a case of epilepsy.

Five cases had experienced phenomena of an hallucinatory nature both auditory and visual. Amnesic phenomena were present in 5 cases.

The border-line type of dysrhythmia we have called epileptoid appears then to be related to the type of border-line fit long ago described as hystero-epilepsy.

(c) The epileptic group exhibited the features common to all such groups and in addition had attacks of *petit* or *grand mal*. They also suffered from "fits" somewhat similar to those reported in the epileptoid groups but which clinically had been definitely recognized as true epileptic automatism. Here is an example.

The patient, a boy of 16, "suddenly, whilst reading, gets up, rushes upstairs, bows his head, screws his face, then falls down and passes right out for twenty minutes. On recovering, he does not speak and has a long sleep. He then says that he has had a feeling of flying into the air".

This group did not show hallucinatory phenomena but in some cases there were such phenomena as indescribable taste in the mouth, unpleasant feeling in the stomach, feeling of being back in the past, sensation of time suspended, recurrent moments of elation or ecstasy, aura of word association. One patient experienced an aura when he felt the presence of somebody standing behind him and to his left which after months of observations we regarded as a disturbance of the body image.

**EEG patterns and intelligence tests.**—Intelligence tests were given to a number of these patients, and included performance and verbal tests. The tests used were the Raven Progressive Matrices, the Mill Hill Vocabulary and the Wechsler (both the performance and verbal scales). The results are shown in Table I. The epileptoid and epileptic cases

TABLE I

| Constitutional |     |      | Epilepsy |     |      | Constitutional |     |      | Epilepsy |     |      |
|----------------|-----|------|----------|-----|------|----------------|-----|------|----------|-----|------|
| RPM            | MHV | D    | RPM      | MHV | D    | WP             | WV  | D    | WP       | WV  | D    |
| 81             | 86  | + 5  | 122      | 115 | - 7  | 110            | 111 | + 1  | 124      | 129 | + 5  |
| 110            | 112 | + 2  | 90       | 81  | - 9  | 80             | 89  | + 9  | 102      | 79  | - 23 |
| 83             | 76  | - 7  | 92       | 81  | - 11 | 80             | 102 | + 22 | 76       | 72  | - 4  |
| 120            | 124 | + 4  | 96       | 94  | - 2  | 82             | 84  | + 2  | 96       | 99  | + 3  |
| 114            | 111 | - 3  | 98       | 76  | - 22 | 110            | 126 | + 16 | 103      | 84  | - 19 |
| 106            | 146 | + 40 | 95       | 76  | - 19 | 113            | 135 | + 22 | 115      | 94  | - 21 |
| 96             | 100 | + 4  | 79       | 66  | - 13 | 112            | 95  | - 17 | 107      | 89  | - 18 |
| 114            | 127 | + 13 | 104      | 106 | + 2  | 97             | 106 | + 9  | 112      | 102 | - 10 |
| 104            | 103 | - 1  | 99       | 114 | + 15 | 118            | 131 | + 13 | 92       | 70  | - 22 |
| 96             | 115 | + 19 | 108      | 110 | + 2  |                |     |      | 84       | 76  | - 8  |
| 78             | 103 | + 25 | 94       | 96  | + 2  |                |     |      |          |     |      |
| 98             | 111 | + 13 | 82       | 84  | + 2  |                |     |      |          |     |      |

## Beta Activity

|     |     |      |
|-----|-----|------|
| 86  | 106 | + 20 |
| 106 | 130 | + 24 |
| 120 | 124 | + 4  |
| 95  | 97  | + 2  |
| 88  | 106 | + 18 |

Abbreviations  
 RPM = Raven's Progressive Matrices  
 MHV = Mill Hill Vocabulary  
 WP = Wechsler Performance  
 WV = Wechsler Verbal

have been grouped together (with the exception of the 5 cases showing runs of beta activity only) under the heading "Epilepsy".

When the scores on the verbal and performance scales are compared in each group it is found that in the Constitutional group the verbal scores tend to be higher than the performance scores, whilst in the Epileptic group the reverse tendency is observed. The 5 cases showing runs of beta activity as the only other abnormality present, apart from the non-paroxysmal slow activity (i.e. no paroxysmal slow and fast activity, sharp waves or spikes), behave as the Constitutional group. The possible meaning of these findings will be discussed later.

#### PART II.—ACQUIRED CASES

23 cases of acquired lesion of the temporal lobe were collected. Of these 6 were tumours and another 2 are under investigation and thought to be tumours. 5 are post-traumatic cases, 1 is an encephalitic, 1 is a case of eclampsia, 5 are cases diagnosed as cortical atrophy of doubtful origin. Of the tumours 6 out of 8 were on the right side, 1 was bilateral and 1 on the left. Of the traumatic cases, 1 was on the right (a depressed fracture) and 4 were on the left (no localized fracture), the 5 cases diagnosed as cortical atrophy of unknown origin are all left-sided abnormalities. 5 of the tumour cases were verified at operation or post-mortem.

*Symptomatology.*—These cases were admitted to the Maudsley because they were suffering from mental symptoms. The main features are summarized as follows:

(1) In all cases there were gross personality changes. These patients became less sociable, irritable and in some cases quarrelsome. Their capacity for work became impaired. Often their behaviour was described as hysterical; 2 cases were actually diagnosed as hysteria; in 3 cases a definite schizophrenic impression was produced.

(2) Hallucinations, auditory and visual, were present in 7 cases.

(3) Amnesia, memory defect and disorientation were present in some cases.

(4) Epileptic equivalent includes feeling of *déjà vu*, visions of past events, sensation of elation, or ecstasy, and also major and minor fits.

(5) In 2 cases the patients episodically experienced the sensation that somebody was standing behind them. This is a symptom that we have observed three times and which we would like to relate to a disorder of the body image.

We have found similarity in many ways between the symptomatology of the cases with acquired lesions of the temporal lobe and those cases selected on the basis of the presence of an EEG abnormality in the same area with no known acquired lesion. Here are two examples:

A woman of 60 is described as having been "always cheerful, sociable, fond of company and outdoor activity, busy with her home and visiting friends. At the age of 58 she started having turns in which she would suddenly go pale, stop talking and then make queer irrelevant remarks. She became very irritable and querulous and ill-tempered, unsociable and unfriendly and lost interest in her social activities. Her memory showed marked deterioration and she tended to become careless in her clothes and appearance." She was fully investigated and the diagnosis of Alzheimer's disease made. At post-mortem a well-encapsulated meningioma pressing on the left posterior inferior part of the temporal lobe was found.

A man of 32 was admitted complaining of headache and loss of power of concentration. There had been nothing in his past history except for some possible mild psychopathic personality traits. In the hospital his behaviour was grossly hysterical and very dramatic. His gait was unstable when in front of people; during a medical conference he addressed the doctors in a very histrionic way with dramatic affirmation that he was not putting up a show. His memory was bad only for some events that had got him into trouble in the Air Force, but when pressed he could remember them fairly well. He made approximate answers to questions in a way which was reminiscent of a Ganser state. Every investigation on this case remained negative. He died in the ward and he had a diffuse glioma on the right side which involved the right temporal lobe and extended to the ventricles.

#### PART III.—INTERRELATIONSHIP OF FACTORS OF SEX, EEG TYPES AND LATERALITY OF EEG ABNORMALITY

The group of 59 cases of "non-acquired" cases were examined statistically for any possible correlations between sex, EEG types and laterality of EEG abnormality (Table II).

For the sake of statistical analysis the epileptoid and epileptic EEG types were grouped together under the common heading of epilepsy. This group therefore consists of all those records which showed activity of a paroxysmal nature (i.e. paroxysmal fast and slow waves, sharp waves and spikes). The constitutional group has been described previously.

Several statistically significant correlations were arrived at which can be summarized as follows:

(a) Irrespective of the type of EEG abnormality there is a higher percentage of right-sided abnormality in males than females.

TABLE II.—TABLE SHOWING NUMBERS OF NON-ACQUIRED TEMPORAL CASES DIVIDED ACCORDING TO TYPE OF RECORD, LATERALITY OF ABNORMALITY AND SEX OF PATIENT, WITH RELEVANT STATISTICAL CORRELATION (BY FISHER'S MODIFICATION OF  $X^2$ )

**Constitutional**

**Male**

R  
13

L  
5

**Female**

R  
6

L  
1

**Epileptic**

**Male**

R  
9

L  
9

**Female**

R  
1

L  
15

**Total 59**

|                        |                | Right | Left |                                        |
|------------------------|----------------|-------|------|----------------------------------------|
| Both<br>sexes          | Constitutional | 19    | 6    | $X^2$ Significant at 1% level          |
|                        | Epileptic      | 10    | 24   |                                        |
| Both<br>EEG types      | Male           | 22    | 14   | $X^2 = 5.5$<br>Significant at 1% level |
|                        | Female         | 7     | 16   |                                        |
| Epileptic<br>EEGs      | Male           | 9     | 9    | Significant at 5% level                |
|                        | Female         | 1     | 15   |                                        |
| Constitutional<br>EEGs | Male           | 13    | 5    |                                        |
|                        | Female         | 6     | 1    |                                        |

(b) Irrespective of sex, the epileptic abnormality tends to be more common on the left than on the right.

(c) Within the epileptic group, though the EEG abnormality is more common on the left in both sexes, nevertheless there are significantly more right-sided epileptic EEGs in males than in females.

(The statistical analysis of the data was carried out by a method suitable for a small number of cases.)

Table II illustrates the above results.

In order to obtain further confirmation of these findings we again went through some 2,000 EEG reports and selected all those cases of the non-acquired type which showed lateralization of the EEG abnormality without localization in the temporal lobes. The total number of records was similarly analysed statistically and the same conclusions were reached as in our first group. The results are shown in Table III.

TABLE III.—TABLE SHOWING NUMBER OF NON-ACQUIRED CASES WITH ABNORMALITY MAINLY OR SOLELY ON ONE SIDE BUT NOT LOCALIZED TO THE TEMPORAL AREA, DIVIDED ACCORDING TO TYPE OF RECORD, LATERALITY OF ABNORMALITY AND SEX OF PATIENT WITH RELEVANT STATISTICAL CORRELATION

Constitutional

Male

R  
26

L  
9

Female

R  
12

L  
13

Epileptic

Male

R  
31

L  
45

Female

R  
13

L  
42

Total 191

|                     |                | Right | Left |                                |
|---------------------|----------------|-------|------|--------------------------------|
| Both sexes          | Constitutional | 38    | 22   | $X^2 = 14.8$                   |
|                     | Epileptic      | 44    | 87   |                                |
| Both EEG types      | Male           | 57    | 54   | $X^2 = 7.9$                    |
|                     | Female         | 25    | 55   |                                |
| Epileptic EEGs      | Male           | 31    | 45   | Significant at 1% level        |
|                     | Female         | 13    | 42   |                                |
| Constitutional EEGs | Male           | 26    | 9    | $X^2 = \text{non-significant}$ |
|                     | Female         | 12    | 13   |                                |



The meaning of these results will now be considered :

#### DISCUSSION

(a) The clinical findings in cases having an EEG abnormality in the temporal lobes and those having an acquired lesion in the same regions have been found to be in many ways similar and have been described. It will be useful to discuss these findings with regard to previously reported manifestations of temporal lobe lesions in the literature. Certain symptoms in our cases such as the hallucinations, the dreamy states and the amnesias are too well known to deserve comment. Other symptoms found in our cases have not, however, been commented upon so frequently. Kennedy Foster as early as 1911 had commented on the peculiar type of anxiety associated with uncinatc seizures. Lately David and Askénasy (1937) have laid stress on this symptom as associated with tumours of the temporal areas. It is interesting to note that several of our epileptic cases have experienced this sensation as an aura, whilst the non-epileptic ones experience it less episodically and more diffusely. Gibbs *et al.* (1948) have reported similar observations in psychomotor epilepsy with a focus located in the temporal lobes.

Another less commonly noticed symptom is aggression and irritability. Sjöqvist (1941) published the case of a man with attacks of rage who had a large right temporal scar. This man was operated on, and though it was found that the brain damage was temporal with no signs of involvement of other regions, and though the attacks of rage ceased after operation, Sjöqvist himself related the rage attacks to the hypothalamus. Hill (1944) found that his most violent and aggressive psychopaths had inferior right temporal EEG foci.

In an article now in press, Dr. D. L. Davies has found in a group of cases of Friedreich's ataxia similar findings as those of Hill in cases showing aggressive tendencies. Irritability had been noticed by previous observers in Friedreich's ataxia but Davies has been able to show that they bear some relation to the presence of EEG abnormality in the temporal areas.

Personality changes are reported by many authors in more recent clinical studies on the temporal lobe. As already mentioned, a summary of such studies by Frantz (1947) is available. However, some authors have been struck by the resemblance of the frontal and temporal lobe syndromes and have failed to see that apart from inevitable resemblances, since we are dealing with personality deterioration, there are also some very real differences. The dreamy states, the hallucinations, the amnesias (as pointed out by Ritchie Russell, 1948) and more especially so far as personality is concerned, the anxiety, the aggression and the irritability are in contrast to the frontal lobe syndrome summarized by Frankl and Mayer-Gross (1947) as euphoria, fatuous equanimity, absence of finer emotional responses, rudeness, tactlessness, hyperkinesis, restlessness, and distractibility. In this connexion it is interesting to note that the posterior orbital plate is now recognized as being foremost in producing the grosser features of personality changes such as the restlessness and hyperkinesis, as was well shown by Meyer and McLardy (1948) in their comparison of anterior and posterior leucotomy cuts and it is interesting that the posterior orbital plate is connected to the temporal pole by the uncinate fasciculus.

It has often been pointed out in the literature that one of the distinguishing features of the Alzheimer and Pick's diseases is the relatively higher occurrence of irritability in the former and euphoria in the latter, but it is also known that in Alzheimer's disease, though diffuse, the neuropathological changes are more marked in the temporo-occipital regions as compared with Pick's disease, where the changes are predominantly frontal as well as in the temporal areas. Stengel (1943) comments: "One may conjecture that a leucotomy carried out in a typical case of Alzheimer's disease may change the clinical picture into one very similar to, or even identical with, that of a typical case of Pick's disease."

In a study on psychomotor epilepsy Gibbs *et al.* (1948) write: "In view of the high association of personality disorders with psychomotor epilepsy, it seems reasonable to attribute much of what has been called the epileptic personality to disturbances in the anterior temporal area" (i.e. where Gibbs has located the EEG abnormality). As for the type of personality disorder, he points out that the headings used by the physicians are hysteria, psychopathic personality or schizoid psychosis. Finally we would also like to draw attention to some comments by Ritchie Russell (1948) on the effects of injury in the frontal and temporal areas. He suggests as a result of his observations on trauma in the temporo-parietal regions that in adults the main behaviour patterns seem to be established in these regions.

(b) *EEG patterns and symptomatology.*—We have already demonstrated the association of the three types of EEG patterns with certain clinical manifestations. In particular the epileptoid EEG group where the clinical type of "attack" corresponded to the sort of attack formerly described as hystero-epilepsy.

Though the method of primary selection by EEG data prevents us proving that these

symptoms are unique to the temporal area, we can say with confidence that no "constitutional" focus has ever been seen other than in the temporal lobe, and acquired focal lesions elsewhere tend to show the symptoms clinically to be expected from these areas. We have certainly encountered patients who resemble ours in personality and symptomatology with diffusely abnormal records. In such cases abnormal activity is recorded from the same electrode positions in the cases showing focal abnormality in the temporal areas. Because the electrical activity recorded is of cortical cell activity it seems unlikely that one can assume intact functioning of the temporal cortex in such cases, even though the origin of the electrical disturbance may be elsewhere, e.g. in the basal regions. Kershman (1949) recently described subjects who would correspond in many ways to our so-called epileptoid group in symptomatology. Their records showed diffuse abnormality in the majority of cases, although it is noteworthy that 6 out of the 114 showed foci all in the temporal lobe. He hypothesized a disturbance at the basal end of the cortico-basal circuits which are often assumed to be the origin of bilaterally synchronous disturbances. From our studies it would seem more likely that the cortical end is the abnormal one, otherwise it is difficult to account for the differences between the two sides of the brain.

(c) *Epilepsy and the left side.*—Before passing to our general hypothesis, we should like to mention some evidence which tends to support our findings of epileptic EEGs being more common on the left than right. We are fully aware that our findings that epileptic EEGs are more common on the left depend on our own criteria of epileptic EEGs which may well be questioned. However, significant differences are found when the correlates (clinical, age, sex, side of brain, &c.) of the type of EEG that we have called constitutional are compared and contrasted with the correlates of the combined groups consisting of the epileptic EEGs and what we have called the epileptoid EEGs, i.e. all records showing paroxysmal activity. It is with these limitations in mind and being aware of the difficulties created by terminology that we will try to discuss our findings in relation to previously reported clinical findings in the literature.

Larsby and Lindgren (1940) recently reported on air ventriculography in a hospitalized group of 97 deteriorated epileptics. 26 had asymmetrical ventricles and of these 19 showed the abnormally enlarged ventricle on the left. Boening and Konstantinu (1933) in a similar study also found more left-sided involvement. Thus of 94 cases examined 42 were asymmetrical and the abnormality was found in the left in 28 cases and 12 on the right side.

Reviewing the cases published by Hughlings Jackson in his various writings, we have been struck by the high percentage of his cases showing clinical phenomena on the right not the left side, that is, left-sided brain involvement. He himself remarks after quoting an example of march of spasm on the right side of the body, "I have, I regret to say, no useful observation on the order of spread of the left side". In later years he came back to this subject and said: "I wrote then that I have no useful observations on the order of spread of spasm on the left side. I have since had few answers to these questions."

A very tentative explanation of the intelligence test results which, as already mentioned, show a difference between the constitutional and epileptic groups will now be given. The relation between the epileptoid and epileptic EEG as electro-encephalographically determined, and the left side of the brain, has already been stressed. It is possible that the verbal functions underlying the acquisition of vocabulary which are known to be located on the left side of the brain are in some way disturbed by the epileptic process. It is known that speech disorders are common in deteriorated epileptics. In our cases the difficulty has been in the acquisition of these functions, not their subsequent loss. It is interesting that Wechsler reports that predominance of performance over ability is found frequently in the so-called psychopaths, where there is reason to believe the epileptoid EEGs are more commonly found. Recently, Thurstone (1948) has indicated the possibility of investigating the similarities of such special primary abilities as verbal fluency and verbal facility with specific disturbances of speech in the aphasias. He also quotes the work of Lynn who has found a different symptomatology in patients with high verbal fluency and low space factor and vice versa.

However, it must be remembered that such factors as the degree of dominance, the intensity of the epileptic disturbance, the age at which it started and the education received will all be factors probably affecting these results.

#### HYPOTHESIS

We are now in a position to state our general hypothesis of the nature of these findings, which is briefly, that there is in these patients a defect or lack of maturation in the temporal lobes, more particularly of the posterior temporal areas, seen physiologically in the EEG abnormalities, and psychologically in the clinical picture.

It is well known that the percentage of all EEG abnormalities in all psychiatric material tends to fall with age (e.g. Greenblatt, 1944). Our group chosen in the first place by EEG

criteria is predominantly below thirty. There are 45 cases from ages 11 to 29 and only 14 cases above age 30.

The type of EEG abnormality also shows a relation to age in that the slow delta frequencies are seen only in childhood (unless, of course, they are post-ictal phenomena). These findings accord with those seen in the EEG development of normal children who show dominant delta activity, speeding to theta activity with growth and later the normal adults show traces only of theta rhythm, if any at all. Such findings apply to EEG dysrhythmia whatever their site in the brain. However, in a study of EEG development, Grey Walter and Dovey (1947) find that theta activity disappears last in the temporal regions. They also find that this activity disappears later on the left than on the right. In our total cases there are more left-sided cases than right, especially if one considers that many of the left-sided abnormalities show epileptic phenomena obscuring a probable constitutional defect. The changes in the EEG are exactly similar to the changes that occur in normal children's EEGs, only in the latter they occur at an earlier age. In a number of our cases the EEG was repeated after several months or even years (as long as three years) and in a few cases there was a striking improvement which heralded a change for the better in the patient's behaviour.

The hypothesis of maturation of the temporal areas was, in fact, first put forward by D. Hill, who said in 1942: "In view of the similarity between the aggressive behaviour of psychopaths and the normal bad temper response to frustration in young children on the one hand, and the similarity between the EEGs of aggressive psychopaths and those of young children on the other, the suggestion that the abnormality in EEGs in these cases is produced by a failure of development in the central nervous system is very tempting. As, however, many problem children do not become psychopathic adults, one must suppose that a process of maturation does generally occur, but in some cases may be delayed and in some may never be complete."

It is interesting here to give some consideration to the phylogeny and ontogeny of the temporal lobes. Phylogenetically this region shows the highest development in man as compared with lower animals—and not as is commonly believed the frontal lobe. Ontogenetically it has been shown by Turner (1948), in a study of the morphological changes taking place in the human brain from birth to adulthood, that the temporo-parietal areas undergo a great increase in size, and complexity in the course of growth and maturation. These changes are normally more or less completed by the age of 10 years, the age at which the adult type of EEG is normally found. It is somewhere near the posterior temporal areas that we have located approximately the EEG abnormality, that is, at the site of maximum developmental changes.

The connexions of the temporal lobe are also worthy of comment. Le Gros Clark (1948) states: "Much of the temporal cortex seems thus to be concerned with the ultimate reception directly or indirectly of the association-fibre systems of other areas of the cerebral cortex and therefore receives the resultants of cortical activity as a whole. This is a matter of particular interest, since (except for the auditory area) the temporal cortex shares with the insular cortex the distinction of having no apparent projection systems from the thalamus and herein contrasts rather strongly with most other areas of the cortex." It is thus in a peculiarly appropriate position for being the centre of the highest integration of cortical activity.

Two further facts enable us to extend our hypothesis slightly to provide a possible explanation of the finding of more right abnormalities in males than females. It is known that males mature in many somatic functions about eighteen months later than females—the literature is well summarized in Carmichael's Text Book of Child Psychology. There is also evidence that there are more behaviour problem and delinquent boys than girls and also more male mental defectives, according to some authors. Grey Walter, as we have already said, finds the right side matures earlier than the left. Therefore, if boys mature later than girls there will be more right-sided immaturity in boys as compared with girls at a certain age. Moreover, if more males remain immature than females, this tendency will be still further increased. Of course, we offer no explanation for the fact of fewer boys maturing and maturation being later than in girls.

An analysis of variance was done on the ages of the patients in the various sub-groups of our material. It showed that there were statistically reliable differences in average age between the various diagnostic groups. This having been ascertained, if we now compare the actual mean for the ages of the various groups, we find that the mean for the right constitutional female group is sixteen months younger than the right constitutional male group; the left constitutional male group is seven years older than the right; no figures are available for the left female constitutional group. Also, the total number of constitutional males is greater than the female number. Thus, these findings are in full agreement with both hypotheses put forward as an extension of our maturation hypothesis.

## SUMMARY

These patients may therefore be viewed as showing a lack of physiological maturation at the highest level which may be compared with their psychological immaturity. They are children in their EEGs and in their personalities, though chronologically grown up. Whereas lesions of the temporal lobes produce similar symptoms by loss of function and release of lower levels of integration these patients have never acquired the highest integration and therefore present a picture similar in certain respects, though, of course, differences are bound to exist in view of the unequal dissolution of already acquired functions.

We hope that this study will be a small contribution to some of the factors determining constitution, more especially the part played by the temporal lobe in the making of personality, temperament, and intellectual functions of man.

Finally, we have to thank various members of the Psychology Department, especially Miss Israëls, for carrying out many of the tests, Mr. A. Lubin for the statistical analyses, and Dr. J. W. Lovett Doust for doing the somatyping and personality and other tests. How much we owe to Dr. Denis Hill is apparent throughout this paper, but we have also to thank him for his constant help and encouragement.

## REFERENCES

- BOENING, H., and KONSTANTINU, N. U. (1933) *Arch. Psych.*, 100, 171.  
 CLARK, W. E. LE GROS (1948) *Lancet* (i), 353.  
 DAVID, M., and ASKÉNASY, H. (1937) *Encéphale*, 1, 169.  
 FOSTER, KENNEDY (1911) *Arch. int. Med.*, 81, 317.  
 FRANKL, L., and MAYER-GROSS, W. (1947) *Lancet* (ii), 820.  
 FRANTZ, R. (1947) *Bull. Los Ang. Neurol. Soc.*, 12, 150.  
 GIBBS, E. L., GIBBS, F. A., and FUSTER, B. (1948) *Arch. Neurol. Psychiat.*, 60, 331.  
 GREENBLATT, M. (1944) *Amer. J. Psychiat.*, 101, 82.  
 HILL, D. (1944) *Proc. R. Soc. Med.*, 37, 317.  
 ———, and WATTERSON, D. (1942) *J. Neurol. Psychiat.*, 5, 47.  
 JACKSON, HUGHLINGS (1931) *Selected Writings*, Vol. 1. London.  
 KERSHMAN, J. (1949) *J. Neurol. Neurosurg. Psychiat.*, 12, 25.  
 KLÜVER, H., and BUCY, P. C. (1939) *Arch. Neurol. Psychiat.*, 42, 979.  
 LARSBY, H., and LINDGREN, E. (1940) *Acta Psych. Neur.*, 15, 337.  
 MEYER, A., and McLARDY, T. (1948) *J. ment. Sci.*, 94, 555.  
 OBRADOR, S. (1947) *J. Neuropath. exper. Neurol.*, 6, 185.  
 RUSSELL, W. R. (1948) *Lancet* (i), 357.  
 SJÖQVIST, O. (1941) *Acta chir. Scand.*, 85, 235.  
 STENGEL, E. (1943) *J. ment. Sci.*, 89, 1.  
 THURSTONE, L. L. (1948) *The Amer. Psych.*, 3, 402 (No. 9).  
 TURNER, O. A. (1948) *Arch. Neurol. Psychiat.*, 59, 1.  
 WALTER, W. GREY, and DOVEY, V. J. (1947) *EEG. Soc. Proc.* (unpublished).

## Section of Pædiatrics

President—Professor J. M. SMELLIE, O.B.E., M.D., F.R.C.P.

[April 22, 1949]

### DISCUSSION: TOILET TRAINING IN EARLY CHILDHOOD

Mr. Adam Curle (*Tavistock Institute of Human Relations*) [*Short Version*]: A comparative study of society reveals some congruity between the wider social forms and techniques of habit formation, and it becomes evident that these last are associated with changes and variations in the broadest social outline.

At the risk of generalization, I would suggest that analysis of certain primitive societies shows a correlation between five variables: an insistence on personal cleanliness; early and forced weaning; deprivation of maternal care; a pattern of adult behaviour in which conflict and aggression are more dominant than friendly co-operation; and personality features which we would consider as psycho-pathological.

Nevertheless, the primitive is so integrated with his society that it may even make use of behaviour which, with us, might be dangerous to familial and group cohesion. Intense aggression, for example, if it be canalized and directed outwards, can actually cement the unity of a tribe.

In addition to other sociological forces, there are two main psychological media which knit the primitive into the fabric of his culture. The first of these is social consistency, by which I mean a continuity of behaviour patterns carried through from childhood into adult life. The second is the emotionally very cogent initiation ceremony, by means of which, in societies in which behaviour patterns traditionally alter with advancing years, the child is helped over the transition periods of his growth. It is interesting to note that in the more consistent societies this ceremony has little more importance than a birthday party in our own.

I make this excursion into primitive society in order to show that the socially traumatic effect of the five variables already mentioned may be minimized by certain traditional mechanisms.

As regards our own society, it is even more dangerous to generalize, but whatever our techniques for obtaining cleanliness, either through punitive sanctions or the gentle means of persuasion and reward, it is clear that we hold it as a definite end in view, and in this we differ from other primitives who insist on no training whatever. In such societies the children receive a large measure of maternal care and affection, are not abruptly weaned, and eventually pass on to a maturity marked by co-operation rather than by conflict.

Judged in this light, our own attitude towards habit training seems to lie somewhere between these two extreme primitive attitudes, and although it is outside my scope to suggest how far our attitude towards weaning, feeding, &c., is consistent with our ideas about evacuation, I would say that we have come increasingly to rely on the somewhat artificial methods of the more "neurotic" primitive societies.

Have we, on the other hand, the same mechanisms for dealing with the difficulties which may follow on from these methods? Have we anything to correspond with the primitive initiation ceremony? The religious Confirmation ceremony would roughly parallel this, but the force and purpose of this ceremony have been very largely allowed to lapse. Again, how far is our society consistent? Parts of it are, certainly, but looking a little farther, we discover such unrealities as the myth that children are unconscious of sex, and the violent launching forth of the child, hitherto regarded as helpless and irresponsible, into the lonely battles of an economic world.

Such a cleavage would certainly account for part of the disturbances affecting young people starting work, and even for the high incidence of schizophrenia at this age. Other equally significant inconsistencies could, of course, also be mentioned, and to my mind we have at our disposal few means of reconciling them.

## SUMMARY

These patients may therefore be viewed as showing a lack of physiological maturation at the highest level which may be compared with their psychological immaturity. They are children in their EEGs and in their personalities, though chronologically grown up. Whereas lesions of the temporal lobes produce similar symptoms by loss of function and release of lower levels of integration these patients have never acquired the highest integration and therefore present a picture similar in certain respects, though, of course, differences are bound to exist in view of the unequal dissolution of already acquired functions.

We hope that this study will be a small contribution to some of the factors determining constitution, more especially the part played by the temporal lobe in the making of personality, temperament, and intellectual functions of man.

Finally, we have to thank various members of the Psychology Department, especially Miss Israëls, for carrying out many of the tests, Mr. A. Lubin for the statistical analyses, and Dr. J. W. Lovett Doust for doing the somatotyping and personality and other tests. How much we owe to Dr. Denis Hill is apparent throughout this paper, but we have also to thank him for his constant help and encouragement.

## REFERENCES

- BOENING, H., and KONSTANTINU, N. U. (1933) *Arch. Psych.*, **100**, 171.  
 CLARK, W. E. LE GROS (1948) *Lancet* (i), 353.  
 DAVID, M., and ASKÉNASY, H. (1937) *Encéphale*, **1**, 169.  
 FOSTER, KENNEDY (1911) *Arch. int. Med.*, **81**, 317.  
 FRANKL, L., and MAYER-GROSS, W. (1947) *Lancet* (ii), 820.  
 FRANTZ, R. (1947) *Bull. Los Ang. Neurol. Soc.*, **12**, 150.  
 GIBBS, E. L., GIBBS, F. A., and FUSTER, B. (1948) *Arch. Neurol. Psychiat.*, **60**, 331.  
 GREENBLATT, M. (1944) *Amer. J. Psychiat.*, **101**, 82.  
 HILL, D. (1944) *Proc. R. Soc. Med.*, **37**, 317.  
 —, and WATTERSON, D. (1942) *J. Neurol. Psychiat.*, **5**, 47.  
 JACKSON, HUGHLINGS (1931) *Selected Writings*, Vol. 1. London.  
 KERSHMAN, J. (1949) *J. Neurol. Neurosurg. Psychiat.*, **12**, 25.  
 KLÜVER, H., and BUCY, P. C. (1939) *Arch. Neurol. Psychiat.*, **42**, 979.  
 LARSBY, H., and LINDGREN, E. (1940) *Acta Psych. Neur.*, **15**, 337.  
 MEYER, A., and McLARDY, T. (1948) *J. ment. Sci.*, **94**, 555.  
 OBRADOR, S. (1947) *J. Neuropath. exper. Neurol.*, **6**, 185.  
 RUSSELL, W. R. (1948) *Lancet* (i), 357.  
 SJÖQVIST, O. (1941) *Acta chir. Scand.*, **85**, 235.  
 STENGEL, E. (1943) *J. ment. Sci.*, **89**, 1.  
 THURSTONE, L. L. (1948) *The Amer. Psych.*, **3**, 402 (No. 9).  
 TURNER, O. A. (1948) *Arch. Neurol. Psychiat.*, **59**, 1.  
 WALTER, W. GREY, and DOVEY, V. J. (1947) *EEG. Soc. Proc.* (unpublished).

The fact that it is part of the child's normal emotional development to identify himself with the loved parent makes the whole matter much easier provided the mother pays attention to the normal maturational level and does not urge a standard on the child which is muscularly and psychologically beyond him. A small child naturally, if he is well-loved and secure, seeks to please his mother and discovers that performing in his pot rather than in his bed or his pants receives her approval and is more comfortable to himself. Normally there need not be a great deal of guilt or anxiety about the matter, but this will depend (a) if the mother does *not* show undue concern, disgust or anxiety herself, and (b) if the child is not already disturbed by inner conflicts related to his parents arising from unsatisfactory attitudes of them to him, e.g. rejection.

In bringing up a small child to obtain control of bladder and bowel, my view is that it is a great mistake to pay a lot of attention to the matter. In fact it seems out of proportion to the importance of the subject, perhaps, to bring so many distinguished doctors together to spend an evening discussing the problems of potting! In the first year of life wet and dirty nappies are normal and the pot should not be much in use until the child is twelve months old. After that time it should certainly be offered him, just as his play pen or his high chair was offered at the correct time. Mild satisfaction should be shown at his success, and all adults will find little difficulty in showing this, and mild disapproval may be shown at his failure. Excessive shame or sternness is to be avoided.

Placid but not premature "potting" is in my opinion the best advice.

Dr. R. C. MacKeith asked if Miss Bowley or Mr. Curle could say something about two quite separate aspects. One was that from the mother's point of view: it was all very well not to do anything until the child was 18 months old but there would be an enormous amount of washing to do which could apparently be saved by very gentle training about the age of 6 months. Was it rather a question of whether the technique of training was gentle than at what time it commenced? He would also like to ask how much the method of bowel training was tied up with the intense interest and enormous expenditure by grown-ups in this country on aperients, which he believed was about £40,000,000 a year.

Miss Bowley thought one should put up with the laundry problems in order to prevent the later difficulties. She thought it was wise not to press the training at all until the child was a year old. If the child responded to very gentle suggestion it was all to the good but the best thing was to wait until he was muscularly able to deal with it himself and had a suitable relationship with an adult; at the age of 6 months he had not achieved that.

Dr. I. Hellman said that all knew that cleanliness could be established at an early age. At most hospitals and maternity homes this was done and it worked, as most mothers would admit. In a survey she made a few years ago it was found that in practically all children the response to the cold rim of the vessel produced a reaction which was continuous up to about 4 or 5 months and it lost its automatic response as the intellectual maturation developed. In her statistics 70% of children who were trained on the conditioning level had what was commonly called a "breakdown" somewhere at the end of the first year, that is, between 9 to 14 months old. The automatic response no longer worked and the child had then to learn intellectually what was expected of him and gain conscious control of his sphincters.

It proves extremely difficult to put across to nurses and midwives that early training is undesirable because of the degree of disappointment and anger on the mother's part which brings about a very far-reaching break in the mother-child relationship. The "breakdown" is looked upon as a kind of aggression or at least a deliberate refusal to comply with the mother's request. It was about this time that what was termed obstinacy and tantrums were commonly found and they were often brought about by angry demands made on children who had achieved a previous measure of control. It was very much less dangerous and far more profitable for the child's development to dissuade mothers from using this early conditioning process, although it saved them a great deal of work, and to put across to them just what Miss Bowley quoted from Dr. Hellman's earlier paper, that it was better to wait for the intellectual, muscular and emotional level of maturation which prompted the child to be actively co-operative, which did not arise until 12 to 14 or 15 months.

A difference of opinion between herself and Dr. John Bowlby was largely that Dr. Bowlby thought that the child would learn toilet cleanliness on his own, while her own view was that the child needed some help, the mother's preferably, and a certain mild degree of disapproval showing him quite definitely what was expected from him.

In her statistics she found that whether the training was started at 1 to 2 weeks old or at a later stage, the great majority of children were not clean before 2 years old. This was important because a great deal of energy was wasted and a great deal of the happy relationship between mother and child was ruined between 1 and 2 years. The children whose

Perhaps I may make these points clearer by referring to a section of our own society which I have studied, and which seems to me to have more consistency than is normal amongst us.

The subject of this study was a group of eight isolated, agricultural villages. The child there is made to feel a member of the household from the very beginning, and is always drawn to the centre of every family gathering. Everyone in the village is concerned for him, and lavishes much care and attention on him. In fact, he enjoys a sort of communal care, and finds himself welcome in any house which he may care to enter. His clothes are spotlessly clean and well cared for, and in spite of his riotous good spirits and his friendly and confident manner, he never gives the impression of having been spoiled. On the other hand, the mothers are a constant worry to the district nurse because they will not keep to schedule in feeding, and because they refuse to give any definite habit training. They admit, privately, that they think it wrong to impose standards on their children which they will eventually discover for themselves, in their own good time.

So far as I can tell, this pattern of child rearing is not unique in England, but appears to have been still more prevalent in the past. I do not suggest that we should re-create such a society, which is, of course, linked to many economic anomalies, but I would point out that it illustrates the price we have paid in coinage of emotional disruption for the fruit of industrial civilization.

In primitive society unreasonable emphasis on toilet training is usually associated with other sociological factors which combine to perpetuate a certain personal unbalance.

[Mr. Curle then went on to discuss how such an unbalance may be minimized in a primitive society by various mechanisms, and how we ourselves have failed to provide anything comparable.] I imagine the work being done all over the country by paediatricians may help to reduce some of the traumatic effect of violent habit training, but as a social scientist I would say that this is rather a symptom of a series of interrelated problems which can only be solved by the combined disciplines of all the sciences relating to man's position in society.

**Miss Agatha Bowley:** *Early attitudes to processes and products.*—In early babyhood the child has little or no control. Nature arranges the processes for him. Awareness of sensations in connexion with processes is evident. Sensation of pressure and both pain and pleasure can be noted when the baby passes a motion. The child appears to obtain considerable libidinal satisfaction from the excretory processes and from the excreta itself. Many observers have noted that children of twelve to twenty-four months especially take considerable interest in their excreta and will play with it if permitted. Equally true is it to say that many young children dislike the smell, and the discomfort of wet and dirty pants or beds. Babies often cry through discomfort when left with dirty nappies.

*Psychological treatment* reveals to some extent the infantile attitude to these bodily processes. The young child may feel proud and pleased with the products of his own body. He feels that they are precious, are good gifts to give to his mother. He appears to feel that they have magical properties for good or ill. Primitive communities appear to feel that people can be harmed by their own excreta, or in some instances healed. Very frequently a child seems to regard them as dangerous objects and, in his infantile mode of thinking capable of destroying or damaging the "bad" mother. Experience with maladjusted children supports this view. Soiling and wetting are the natural symptoms of the deprived child. They arise from libidinal satisfactions being withheld and represent the child's attempt to obtain substitute gratifications.

In my experience soiling and wetting, playing with or hiding excreta are not so much characteristics of the mentally defective child, though such a child is slower to gain control than a normal child, but are especially characteristics of the seriously disturbed child. Children from broken homes, children in institutions, children cared for by hated step-mothers frequently show these symptoms. Institutional training does not necessarily bring about an improvement. Punishment aggravates the problem.

What then causes the child normally to achieve habits of cleanliness?

Dr. John Bowlby considers there are two factors at work: (1) the maturational factor; (2) the desire to obtain the mother's approval—identification with the parent's wishes.

It appears that many of the lower animals show evidence of some automatic training. Pigs even use one corner of the sty for defecation. Cats are remarkably fastidious. Margaret Ribble and Benjamin Spock stress the fact that 18–24 months old children train themselves if left to it. The child becomes aware when a movement is imminent, can control it to some extent and will make some sort of signal of his need. If the adult does not respond immediately he will take himself to the proper place for action, probably from watching what other people do. Given opportunity by provision of suitable pots or lavatories, the child naturally makes use of them unless antagonism to his mother or anxiety about the whole process prevents a normal reaction.



She found when she was visiting common-lodging houses that there were in them a number of people who were earning good wages who were reduced to a common-lodging house level because they could not keep their beds clean or because they could not keep their underlinen sufficiently clean.

Doctors were not with children day and night and it was the nurses who had an enormous amount of influence and who were ultimately responsible. She would suggest that the training of nurses in this matter should be looked into and influenced.

The President said that one must not lose sight of physiology. One must remember that there were such things as the gastro-colic reflex and other normal physiological functions which could be encouraged, promoted and trained. Possibly, therefore, bearing in mind these reflexes, some attempt could be made in bowel training during the early months of life without the risk of inflicting any psychological trauma on the infant.

Mr. Adam Curle, in reply, said the answer to the question of how soon primitive children who were not given any particular training became clean was in general that at about the age of 2 they were fairly clean. There were some societies in which no training was undertaken until about 1 year old when it was suddenly started rather intensively but in most of these societies cleanliness was not achieved until 3 or 4. In other societies there was fairly strict habit training from an early age and cleanliness was achieved at varying periods between 18 months and 2½ years, but the data on this subject was so incomplete that generalizations must be taken very guardedly.

The study of primitive societies did pose a question of whether any society with more rich and varied culture could achieve the additional value which existed in primitive societies of the feeling of belonging to the group which shielded the individual from some of the disturbances of change which were more prevalent in modern society than in primitive society.

Miss Bowley, also in reply, said that one speaker had stated that a baby was an automatic machine until it was about 8 months old. That was very contrary to observations she had made of young children. The burden of washing would not be so great or so persistent and continuous if early training was not so insisted upon. If one did gradual training and did not take the matter seriously until the child was a year old relapses were less likely to occur.

[June 11, 1949]

### MEETING AT SOUTHMEAD HOSPITAL, BRISTOL

#### Demonstration of Neonatal Department, Southmead Hospital. [Summary]

Dr. Beryl Corner demonstrated the work of this Department, comprising the nurseries for neonates with 130 cots, and the Premature Unit.

The Premature Unit has 14 cots, six being in a "hot room" adjacent to the labour ward unit, with temperature controlled at 75° F. and humidity 65%. The remaining 8 cots are in two other rooms. The Unit also has its own feed preparation room and a steam autoclave for clothes, bedding, &c. There is a special nursing staff.

During the years 1947 and 1948, 675 premature babies have been treated in the Department, of whom 57 were born outside the hospital. 307 infants were treated in the Premature Unit, the remainder being nursed in ordinary neonatal nurseries. 110 premature infants died, giving a total mortality rate for the series of 16.3%. Of particular interest are the mortality statistics for low birth-weights. In a series of 28 babies with birth-weights less than 2 lb. 8 oz. the mortality rate was 78.5%, and a further 26 infants below 3 lb. had a mortality rate of 57.7%. The figures show the value of subdividing the group of 3 lb.-4 lb. infants, those under 3 lb. 8 oz. having a much lower survival rate than those nearer to 4 lb. at birth, and it is suggested that all statistics for mortality rate according to birth-weight should show this subdivision.

#### MORTALITY RATE ACCORDING TO BIRTH-WEIGHT, 1947 AND 1948

| Weight            | Survived | Died | Total No. | Mortality rate % |
|-------------------|----------|------|-----------|------------------|
| Under 2 lb.       | 3        | 5    | 8         | 62.5             |
| 2 lb.-2 lb. 8 oz. | 3        | 17   | 20        | 85               |
| 2 lb. 8 oz.-3 lb. | 11       | 15   | 26        | 57.7             |
| 3 lb.-3 lb. 8 oz. | 25       | 18   | 43        | 41.9             |
| 3 lb. 8 oz.-4 lb. | 55       | 9    | 64        | 14.1             |
| 4 lb.-5 lb.       | 97       | 19   | 116       | 16.4             |
| 5 lb.-5 lb. 8 oz. | 22       | 2    | 24        | 8.3              |

training was started nearer the 2 years were those whose training did not extend for more than a very few months.

Dr. Lindsey W. Batten said that one had to think of the very real labour involved in washing napkins with the added difficulty that as soon as the child got on to a mixed diet his urine became very irritating and it was extremely common to have children brought along at any age after 8 months with sore genitalia and thighs merely because they had wet their napkins and beds. If they could without psychological damage be persuaded to be a little more dry then it was a great advantage to them and their mother.

When the difficult time came in the second year when the child would roam round the room seated on his pot, insist on not passing his water when taken out of bed at night and then do it five minutes later after being put back, the best thing to do was to take it happily. The child was at the Peter Pan stage, whatever deeper psychological conflicts might be going on; he did not want to grow up—at least, he did not want to grow to the next stage.

If the child was taken up at night he should be awakened so that he felt himself to be doing something positive. Once he got the notion that he was getting up and passing his water and took a satisfaction in having performed for himself that little matter was settled.

Dr. Leslie Housden said that small children were strongly influenced by habits and customs. They reacted to nearly everything that was going on around them and if they had an intelligent mother and one who did not give way to desperation when things did not go quite right, there was little difficulty in bringing them up to pass their urine and faeces where it was best that they should pass them. It might be that most children became wet in their habits and wetted their beds between the first and second years, but it certainly did not occur in his house. One of the things which should be taught to all young people before they had any children at all was a matter of faith—that their infants would be healthy beyond any possibility of doubt, and that they would be born in good working order. He thought it would be a very good thing if the medical profession realized that infants were born in good working order; he would not then have a medical colleague asking what he was to do about his breast-fed daughter who did not pass her motions daily!

What was wrong with habit training was the state of mild panic into which everybody got in trying to enforce cleanly habits instead of just allowing them to happen. If a mother, particularly, was of the right temperament and had had good instruction about infants before her own were born, she would easily train them without any psychological disturbance.

Dr. Portia Holman said that however much one agreed with what Miss Bowley had said about the importance of going slow and not encouraging a mass reflex to start in early months but to wait until there was some cerebral control of the function of excretion, the point of the extra work, and the irritation which it was bound to cause, needed serious and careful consideration. It was not enough to say to the mother, "Put up with the washing", because that might be the last straw which destroyed her health. If this psychological point of view was to be accepted seriously, the consequences had to be considered and one of the most important things from the mother's point of view was that she should be helped with the washing. Nothing was more dispiriting than a house full of washing.

Had some of the members ever been in a working-class house where there was washing in the passages, washing in the kitchen, clothes airing in the front room, and generally a pile of dry and unironed clothes on the floor? Wherever one looked there was evidence of washing any working-class woman's life. That was something which should be dealt with on a communal basis and it seemed to her to be a great lack in our civilization that so many industrial class homes had not been made.

Dr. Letitia Fairfield said that she thought it would be a great mistake to go too far in one direction. Life was not only made for babies, people did grow up and were entitled to some consideration at other stages of their life and there should be mutual balance between the ages. It was not only the washing of the napkins that was such a terrible burden on the mother if this free and easy method was continued too long, but one had also to think of the bed-linen both in institutions and in homes and also of the general standard of cleanliness in the home.

She thought some gentle pressure and direction from adults were needed. If this was not done there was a filthiness and stench in the whole house which lowered the entire standard of living. She had had a lot of experience of having to cope with boys and girls who had been allowed to go to 16 with these habits ignored and the result was that they were almost unplaceable in adult life. It was impossible to get a reasonable emotional, educational or social life for them and if they could not be cured their life was a very sad one.

discussions between all members of the department, no strict dividing line of interest is detectable. The adequate training of a pædiatrician should include a junior resident obstetric appointment during which the fundamentals of obstetric-pædiatric co-ordination will be assimilated, and before reaching consultant status it is highly desirable that some time should be spent as a pædiatric registrar in an obstetric centre.

The joint committee responsible for the recent report on neonatal mortality and morbidity (No. 94 H.M.S.O.) particularly emphasizes the need for study of the newly born baby. The gathering of suitable data for departmental reports on neonatal and maternal results requires that even routine notes must carry accuracy and detail; such records will have, individually or collectively, enormous value in organized schemes for child health study. Something more than a few words in the statement of the antenatal history is necessary if any useful correlation of possible ætiological factors in maternal disorder and foetal abnormality is to be determined.

The alleged realities of the foetal hazards in maternal toxæmia may become more precisely understood where circumstances allow special study of the actual or threatened emergency. It is a valuable instruction to the pædiatrician to be cognizant of the foetal state and to play a significant part in the immediate management of the delivered infant, for we believe that if the foetus is born alive and survives the first few days (which usually means that intracranial hæmorrhage has not occurred) the maternal toxæmia will have no further adverse influence on its life and development. Further detailed studies of the baby born under conditions of toxæmia stress are certainly worthy of a team interest in the neonatal department.

The advancing complexities of analgesia and anaesthesia in obstetric performance are of special concern at the moment, both in regard to the functional value in maternal relief and the possible direct or indirect effects upon the foetus. This calls for further interest in the pharmacological action and the placental transmissibility of drugs in premedication and the additive or synergic influences of anaesthetics. There is evidence indicating that safe anaesthesia in obstetrics implies an awareness of any special susceptibilities of the foetus. Observations made in the labour room on the neonatal respiratory state or other physiological disturbances are necessary in a detailed study of the contributory effects of the various anaesthetic drugs, especially where possible combinations of circumstances are conducive to asphyxial or apnoeic disturbance. Emergency relief of inhalational obstructions may be related to these events and indeed is another important field of joint interest and quick action, including a sure skill in endotracheal clearance and possibly bronchoscopic suction; the anoxic infant cannot wait, or be satisfied with oxygen deflected into an impassable respiratory tract.

Whilst it is clear that most maternity centres are, or will be, blessed with these several and joint services, the availability of special pædiatric emergency facilities for the newborn in domiciliary practice, and most especially for premature babies, will require some cordial discussion between the centre and the general practitioner obstetric services in the area and the peripheral maternity units.

The aim and object of all concerned is to enable the newborn to conserve its "capital of vitality", and in these days of population problems emphasis is towards quality and not quantity. The exhilarating influence of obstetric skill and its encouragement to the trainee in pædiatrics and infant health are never to be undervalued and indeed should be sought after and highly appreciated. We may venture to hope that thoughtful surgeons and physicians sometimes find illumination in joint clinical discussion, so our obstetric and pædiatric sections and societies might consider it something more than a mere academic matter to meet and take up a line of co-ordinate discourse, and not least so in regard to the pressing and advancing liaison in relation to such matters as antenatal pædiatric problems, neonatal asphyxia, the immediate and remote effects of birth injury, and the possible role of drugs used in labour. Specialism cannot exist in isolation; affinities must be maintained between the conventionally sectional departments.

## MEETING AT THE CHILDREN'S HOSPITAL, BRISTOL

### CASES

I.—*Œsophageal Hiatus Hernia with Ulceration of Lower Third of Œsophagus*.—A. V. NEALE, M.D., and R. H. R. BELSEY, M.S.

J. E., boy, born 29.11.45.

*History*.—Well until 2 years of age, then developed habit of throwing back head and holding it over to the left in the fully extended position. Nine weeks later began to have small vomits after meals.

Nov.—PÆDIAT. 2

An analysis of the causes of death in the 3-4 lb. weight group is worthy of special study.

Since January 1947, 54 babies were admitted to the Premature Unit weighing 3 lb.-3 lb. 7 oz. (inclusive) at birth. 22% of these were born before arrival of the midwife and the total mortality rate was 42.6%. The following were the principal causes of death:

| Cause of death                         | No. of cases (1947-May 1949)         |
|----------------------------------------|--------------------------------------|
| Intracranial hæmorrhage .. ..          | 6 (2 born before arrival of midwife) |
| Asphyxia .. ..                         | 5                                    |
| Infection .. ..                        | 2                                    |
| Unexplained (no post-mortem performed) | 2                                    |

No post-mortem abnormality was found in 5 cases, 1 of which died on the second day and the other 4 between the third and seventh days. In 2 further cases dying in the second week intense bile-staining of the basal ganglia was the only abnormal finding. These 7 cases presumably died from metabolic insufficiency.

During the same period, 81 babies weighing 3 lb. 8 oz. to 3 lb. 15 oz. (inclusive) were admitted. 12.3% of these infants were born before arrival of the midwife, of whom 26.6% died, the total mortality rate for this group being 18.5%. The following were the principal causes of death:

| Cause of death                | No. of cases (1947-May 1949)            |
|-------------------------------|-----------------------------------------|
| Intracranial hæmorrhage .. .. | 10 (2 born before arrival of midwife)   |
| Asphyxia .. ..                | 2 (both born before arrival of midwife) |
| Infection .. ..               | 2                                       |
| Hæmolytic disease .. ..       | 1                                       |

There were no unexplained neonatal deaths.

Comparison of these two groups shows the hazards of unattended birth in the larger babies and the high proportion of deaths from presumed metabolic inadequacy in the lower weight group.

These figures also stress the necessity of special care for these small babies, so that in each clinical area there should be a premature department in the principal maternity hospital where the pædiatricians, in collaboration with the obstetricians, can study the particular problems affecting survival in the premature.

In the other neonatal nurseries, of particular interest has been the endeavour to reduce infection. Infants are nursed in cots of the Sorrento type and all toilet other than bathing is carried out in the cot, with the infants' own toilet accessories, including individual ointment jars. Wrapping blankets are enclosed in pillow cases and are only used when the infant is taken out of the cot for feeding. Strict isolation is instituted at once for even the trivial infections. In the last 1,232 live births the incidence of infection has been reduced to 7.4% and, although the total number of cases is smaller, this is a striking reduction from the figures previously given by Corner in 1946 for this hospital (*Proc. R. Soc. Med.*, 39, 383: Hospital B, 3,190 patients, infection rate 29.7%).

#### Professor A. V. Neale, M.D.: Obstetric-Pædiatric Relationships. [Summary]

An increasing realization of the importance of the great initial endeavours of J. W. Ballantyne has led obstetricians, especially in teaching hospitals, conscientiously to desire that undergraduate and post-graduate students should receive extended teaching in the physiology and disorder of the newborn in so far as it is in essence an unbroken chain of thought extending from the antenatal, through the intranatal to the postnatal periods. The many advances in foetal and neonatal physiology have aroused great interest among pædiatricians and a natural desire to apply their extensive knowledge of infancy to this early age-group where mortality and morbidity are still so great.

To ensure respective and respectful co-operation between obstetricians and pædiatricians, the obstetrician quite rightly wants to be assured of two things: (a) That the pædiatric and the obstetrical interests and responsibilities are convergent and not divergent in the team; (b) that the pædiatric staff is deeply interested in the newborn baby and is able to offer special judgments and skills in the particular management. The responsibility of the pædiatrician in the neonatal department carries with it the necessity for projecting an interest into the minutiae of clinical assessment, backed by sound knowledge of the extremely labile physiology of the first few days of life; he must also be prepared to maintain a constant interest in the particular problems of the obstetrician. These reasonable and justifiable assumptions may be regarded as the principles which should govern further general development in the staffing of maternity departments.

The obstetric and pædiatric consultants in maternity centres should encourage a proper integration of function between their respective resident officers, thus affording a dual system of departmental education. The personal contacts should be such that in regular



FIG. 3.

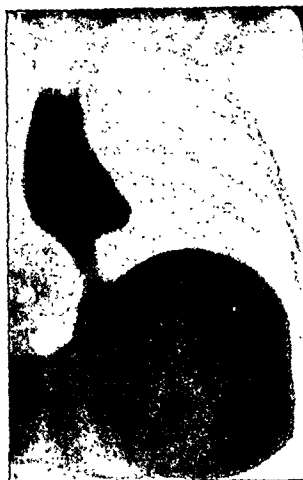


FIG. 4.

FIG. 3 (*Case II*).—Barium meal and swallow showing the large dilatation at the lower end of the oesophagus.

FIG. 4 (*Case III*).—Pre-operative barium meal showing the large dilatation at the lower end of the oesophagus with gastric rugæ extending above the diaphragm.

### III.—Oesophageal Hiatus Hernia.—A. V. NEALE, M.D., and R. H. R. BELSEY, M.S.

R. C., boy, born 1.3.49. Admitted to hospital 21.3.49.

*History*.—Vomiting since birth, sometimes projectile, sometimes regurgitant, with failure to thrive.

*Examination* (21.3.49).—A dehydrated puny baby with thrush. Weighed 4 lb. 10 oz. (birth-weight 6 lb.). No other clinical abnormality found.

*Treatment and progress*.—Fed for eight days by gastric drip; he gained a little weight but no improvement followed. A barium swallow and meal then (6.4.49) revealed an oesophageal hiatus hernia (fig. 4). Treated medically for seven weeks he gained 2 lb. 2 oz. in weight but his vomiting continued. Occult blood was found consistently in the stools during the last four weeks and the hæmoglobin slowly fell. Operation for repair of hernia was performed on 1.6.49 since when he has made fair progress and the vomiting has seldom amounted to more than an occasional regurgitation.

### IV.—Congenital Hiatus Hernia.—BERYL CORNER, M.D., and R. H. R. BELSEY, M.S.

C. D., girl, aged 2 years.

*History*.—The child had suffered from persistent vomiting from birth together with recurring chest infections and had failed to thrive. At the age of 4 weeks she was admitted to a local hospital where she was initially treated for gastro-enteritis and subsequently for pyloric stenosis. Occult blood was constantly found present in the stools and the symptoms defied all therapy. At the age of 9 months she was transferred to Bristol. She then weighed 9 lb. (birth-weight 7 lb.), appeared very dehydrated and there was dullness over the right side of the chest. An X-ray at this time showed a large bilateral hernia through the oesophageal hiatus.

*Treatment and progress*.—On 1.4.48 a left thoracotomy was performed when the hernia was reduced and the oesophageal hiatus reconstructed. The large hernial sac was found lying in the posterior mediastinum and projected into both pleural cavities. It was composed of both pleura and peritoneum and when opened was found to contain the whole of the stomach and a considerable portion of the small intestine. Convalescence was uneventful. The child weighed 12 lb. when 1 year old and 20 lb. at 18 months. She subsequently failed to maintain this rate of progress, however, and when X-rayed in February 1949 was found to have a recurrence of the hernia on the left side (see fig. 5). She was readmitted to hospital and a second repair operation was performed on 29.4.49 with satisfactory results (see fig. 6, 9.6.49).

*Examination findings and progress.*—First admitted to hospital on 28.1.48, aged 2 years. No abnormality was found on this occasion and he was discharged home symptom-free, a few days later. Readmitted in June 1948. An œsophagoscopy then revealed ulceration at the lower end of the œsophagus. His condition responded slowly to medical treatment on this and one further occasion, though he never became completely symptom-free.

In January 1949 at the age of 3 years, he was readmitted for the fourth time, very anæmic, vomiting frequently and suffering from bouts of substernal pain which appeared to be partially alleviated by throwing back the head. On 22.3.49, following transfusion, an operation was performed in which the left phrenic nerve was crushed, the œsophageal mediastinal adhesions freed and the pouch of the stomach lying above the diaphragm drawn down below it. An excellent operation result has been obtained. The boy, symptom-free, is now making good progress on a normal diet. Figs. 1 and 2 show the condition before and after operation.



FIG. 1.



FIG. 2.

FIG. 1 (*Case I*)—Pre-operative barium swallow showing the hiatus hernia with gastric rugæ extending up into the thorax.

FIG. 2 (*Case I*)—Barium swallow after repair of hiatus hernia showing result obtained.

## II.—Œsophageal Hiatus Hernia.—A. V. NEALE, M.D.

S. T., girl, born 14.4.49. Admitted to hospital aged 7 days.

*History.*—Frequent small vomits from birth, associated with occasional cyanotic attacks.

*Examination* (21.4.49).—Child weighed 5 lb. 9 oz. (birth-weight 6 lb. 11 oz.). Her general condition was fair and no abnormality was detected on ordinary clinical examination.

*Treatment and Progress.*—For the first five days in hospital the baby was fed on expressed breast milk given according to a pyloric ladder schedule on which regime she averaged 5 small vomits per day. A barium meal and swallow (fig. 3) on 28.4.49 showed a large dilatation at the lower end of the œsophagus continuous with the stomach and on further screening a diagnosis of œsophageal hiatus hernia was made. The child was subsequently fed by gastric drip for one week when she gained a little weight, following which she was reintroduced to the breast when she took her feeds well and only vomited 4 times over the course of twelve days. Discharged home, she has subsequently continued to make fairly satisfactory progress.

*POSTSCRIPT.*—Baby weighed 9 lb. 13 oz. at the age of 13 weeks; she was still breast fed and was having only an occasional vomit.

# VI.—Œsophageal Atresia and Tracheo-Œsophageal Fistula.—R. H. R. BELSEY, M.S.

J. O., born 16.12.48.

*History.*—From birth this baby frothed from the mouth, feeds were associated with distressed breathing and abdominal distension became marked when the child screamed.

*Treatment and progress.*—Admitted to the Thoracic Unit 18.12.48 aged 2 days. A diagnosis of œsophageal atresia and tracheo-œsophageal fistula was made, following the introduction of lipiodol through a catheter into the œsophagus (see fig. 9). At an immediate operation the tracheo-œsophageal fistula was closed and an end-to-end anastomosis of the two segments of the œsophagus was performed by the transpleural route. Convalescence was uneventful. Feeds were given by mouth on the third post-operative day starting with sterile water for forty-eight hours, and the child was put to the breast after two weeks. A post-operative barium swallow on 23.2.49 showed no stenosis of the normally developing œsophagus and no evidence of any other congenital abnormalities (see fig. 10).



FIG. 9.



FIG. 10.

FIG. 9 (Case VI).—Hold-up of lipiodol and gas in stomach confirming the diagnosis of œsophageal atresia and tracheo-œsophageal fistula.

FIG. 10 (Case VI).—Post-operative barium swallow showing a normally developing œsophagus.

# VII.—Coeliac Disease in Twins.—BERYL CORNER, M.D.

Jean and June L., aged 3 years.

When admitted to hospital aged 15 months they both presented severe clinical pictures of coeliac disease.

*Previous history.*—Healthy children, birth-weight 5 lb. 6 oz., and 5 lb. 8 oz. Fed on National Dried Milk and weaned at 9 months. They developed bronchitis at the age of



FIG. 11 (Case VII).—Coeliac disease in twins. Aged 18 months.



FIG. 5.

FIG. 5 (Case IV).—Barium meal showing recurrence of the oesophageal hiatus hernia on the left side.



FIG. 6.

FIG. 6 (Case IV).—Barium meal and swallow after repair of hiatus hernia showing result obtained.

V.—Recurring Left Diaphragmatic Hernia with Intestinal Obstruction by Adhesions.—R. V. COOKE, Ch.M., and BERYL CORNER, M.D.

J. H., girl, aged 4½ years.

*History.*—17.12.44: First admitted to hospital aged 6 weeks, following a week's vomiting. She appeared grey, dyspnoeic, weighed 7 lb. 2 oz. and was diagnosed as a case of obstruction with a left diaphragmatic hernia. At operation the whole of the alimentary tract from the duodenum to the sigmoid colon was found in the left chest with a portion of the ileum about 3 in. long, strangulated. The whole was replaced in the abdomen and the diaphragm repaired with catgut. A good post-operative recovery followed and the child was discharged home breast-fed a week later.

25.9.48: Readmitted to hospital, aged 4 years, with acute intestinal obstruction and recurrence of the diaphragmatic hernia (fig. 7). At laparotomy a band adhesion was found to be obstructing the ileum near the ileocaecal junction. Loops of small intestine, tightly adherent to one another, were also found in the left thorax. These were separated and the child made a good recovery after a stormy convalescence.

20.12.48: The diaphragmatic hernia was repaired again (fig. 8).



FIG. 7.

FIG. 7 (Case V).—Straight X-ray showing left diaphragmatic hernia.

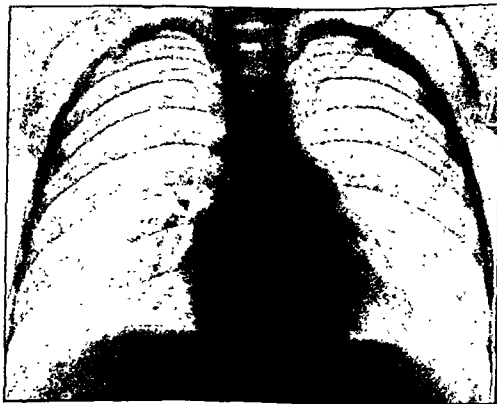


FIG. 8.

FIG. 8 (Case V).—Straight X-ray of chest after repair of diaphragmatic hernia.



**X.—Calcifying Tuberculous Cold Abscess in Left Hypochondrium.**—C. S. SHAW, M.B. (for A. V. NEALE, M.D.).

D. M., boy, aged 3 years. Sent to hospital in 1949 for clinical opinion prior to possible adoption.

*Previous history.*—Was admitted to hospital when 9 months old (April 1947) with tuberculous mesenteric adenitis and rickets. December 1947 underwent block dissection of glands of neck on the right side.

*Examination June 1949.*—A smooth oval cystic swelling, measuring approximately  $2\frac{1}{2}$  inches by 3 inches was found in the left hypochondrium. Fig. 15 shows the extent of calcification.



FIG. 15 (Case X).—Plain X-ray of abdomen showing calcification in a tuberculous cold abscess in the left hypochondrium.

#### DEMONSTRATIONS

**Water and Mineral Metabolism in Newborn Infants and Mammals.**—H. HELLER, M.R.C.P.

The demonstration included (a) urinary osmotic pressure of infants during the first week of life; (b) the effect of posterior pituitary extracts on the urinary osmotic pressure of newborn infants; (c) the hormone content of the human posterior pituitary gland at birth.

**The Histological Changes in the Mammary Gland of the Newborn Infant.**—J. C. VALENTINE, M.B.

This demonstration illustrated the very varied histological appearance in the breast of the newborn. It showed that the breast of the immature infant does not exhibit the same degree of activity as that shown by full-term infants, the mammary gland of the immature infant consisting only of ducts lined by a double layer of epithelial cells.

The mammary gland of the mature infant on the other hand shows a rather variable picture from a simple duct-like arrangement similar to that of the immature baby to a highly complex branching and acinus formation closely resembling the mammary gland of the pregnant woman.

A further type of histological appearance was also demonstrated and this tends to be found in infants dying at a later age than those showing the other histological changes. In this type there is very great distension of the acini with flattening of the epithelium and breakdown of the intervening septa. No definite conclusions as to the significance of this histological appearance have been reached.

**Letterer-Siwe's Disease (Non-lipid Reticulo-endotheliosis) with Diabetes Insipidus but No Bone Changes.**—T. F. HEWER, M.D.

**Pancreatic Heterotopia.**—R. L. BISHTON, M.B., and R. AIDIN, M.D.

Specimens were shown of pancreatic heterotopia in the stomach and small intestine, with and without islets of Langerhans. An example was included of a case of intussusception due to heterotopic pancreatic tissue in the small intestine.

10 months which was followed by mild diarrhoea. The stools subsequently remained pale and were often relaxed and offensive. Loss of weight followed.

*Treatment and progress.*—At 15 months when they commenced treatment they weighed 16 lb. 14 oz. (June) and 18 lb. 6 oz. (Jean). They were given a low fat, low starch diet supplemented with vitamins, iron and liver. They made little progress on this regime at first and at the age of 18 months weighed 18 lb. 2 oz. and 18 lb. 14 oz. respectively (*see fig. 11*), but after six months of treatment they began to gain steadily. Some six and a half months later they were sent from hospital to a convalescent home, weighing 19 lb. 6 oz. (June) and 20 lb. (Jean). On leaving, fourteen weeks later, their weights were 22 lb. 8 oz. and 24 lb. and now, at the age of 3 years, both weigh 28 lb. 8 oz.

#### VIII.—Tuberculous Left Epididymis.—A. WILFRID ADAMS, M.S.

J. H., boy, now aged 10 years. Admitted to hospital aged 8 months with a four-day history of irritability, and swelling in the left scrotum. Micturition was normal and feeds were taken well.

*Family history.*—Father was found to have tuberculosis in 1940, all other members well.

*Examination* (26.3.40).—A well-nourished, fretful child whose left epididymis was swollen, smooth, hard, slightly tender and the overlying skin purplish.

*Investigations.*—W. R. negative; T.B. patch test strongly positive. Urine inoculation into guinea-pig produced widely disseminated tuberculous lesions. Chest X-ray revealed primary tuberculous complex in the right mid-zone. Biopsy of swelling 26.3.40 showed a chronic granulomatous lesion of the epididymis with caseation, epithelioid and giant cells. No tubercle bacilli were seen.

*Treatment.*—Orchidectomy was performed on 23.4.40 and the boy has subsequently made satisfactory progress.

#### IX.—Scurvy, with Bilateral Dislocation of the Lower Femoral Epiphyses.—A. V. NEALE, M.D.

G. C., girl, born 13.2.47. Admitted hospital aged 8 months with three weeks' history of screaming whenever legs were touched or moved.

*Previous history.*—Only child. Given one teaspoonful of ribena daily over four months.

*Examination findings* (3.11.47).—There was extreme tenderness of limbs, the legs being held in the typical fixed position. The gums were swollen and purple.

*Comment.*—The special point of interest in this case was the bilateral dislocation of the lower femoral epiphyses (*see fig. 12*), which have gradually and satisfactorily recovered (*see figs. 13 and 14*), the child being now of normal height.

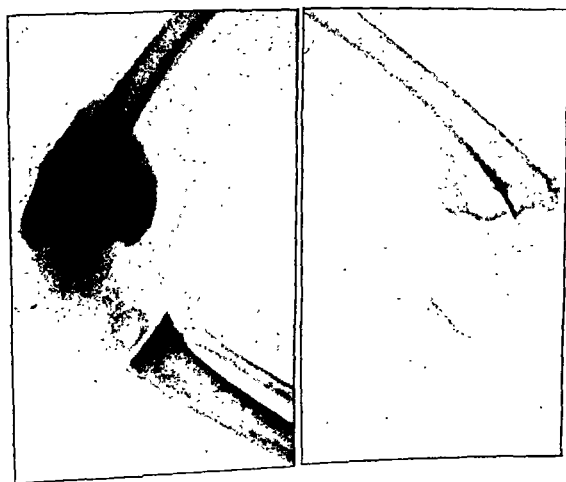


FIG. 12.

FIG. 12 (Case IX).—Subperiosteal hæmorrhages with dislocation of lower femoral epiphyses 18.11.47.

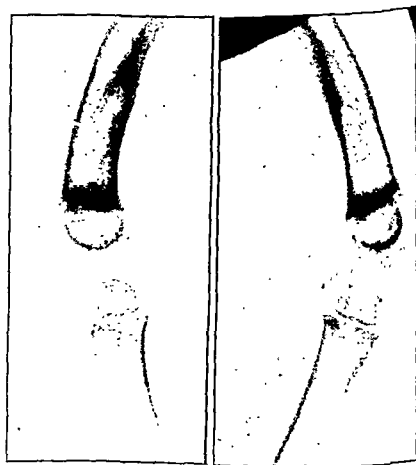


FIG. 13.

FIG. 14.

FIGS. 13 and 14 (Case IX).—Right and left knee-joints after treatment 13.9.48.

growth. Encroachment on the œsophagus must be quite marked to produce effects in the first few months of life, when the diet is exclusively liquid; in milder instances dysphagia or vomiting may therefore occur for the first time when the child is being weaned.

With growth of the trachea and œsophagus both the respiratory and alimentary symptoms tend to recede, and are, as a rule, completely lost by the age of a year or so. The danger of permanent lung damage, if not of death, from supervening infection during this period should, however, be stressed.

#### DIAGNOSIS

A useful clue may sometimes be obtained by auscultation with a stethoscope; the site of maximal intensity of the stridor indicates the site of obstruction in the respiratory tract. In all cases, however, obstruction of the pharynx should be excluded by the usual methods, and radiological investigation, particularly fluoroscopy, is indispensable for diagnosis.

In some instances the vessel itself (e.g. aorta) may be visualized on X-ray screening, or its transmitted pulsations may be observed; but, as a rule, the anomalous vessel is demonstrated indirectly by observation of the œsophagus and trachea.

Screening while a barium mixture is being swallowed brings clearly into view any displacement or compression of the œsophagus. The commonest site is at the level of the third or fourth thoracic vertebra. Fig. 1 shows bilateral compression due to a vascular ring.

Alterations in the course or width of the trachea can be seen in good X-ray films, taken in the postero-anterior and lateral projections. The interpretation of such changes is dependent on a knowledge of the normal variants, which is still incomplete; a study of such variants is being carried out in collaboration with Dr. H. J. Johnson. In doubtful cases, the trachea may be outlined by the instillation of opaque material. Such tracheograms are simple to obtain; the procedure is relatively free from danger, and it is preferable to inspection through a bronchoscope.

In most cases the simple methods described suffice for a perfectly adequate demonstration. In selected cases angiograms give an excellent outline of the course of the vessels. Fig. 2 shows an anomalous right subclavian artery and fig. 3 an aberrant innominate artery demonstrated by this method.

#### TREATMENT

Surgical correction of the anomaly is necessary in only a very small proportion of cases. It is certainly advisable if there is serious difficulty in breathing or swallowing, and further experience will show to what extent the danger of repeated pulmonary infection is an indication for operation.

Operative treatment can be relatively straightforward, and in suitable cases the effects are dramatic and complete. For details the description by Gross and Ware (1946, 1947) should be consulted. A vascular ring may be interrupted by ligating and cutting an unimportant segment, e.g. the narrower limb of a double aortic arch, or the ductus arteriosus (or ligamentum arteriosum) joining a right aortic arch to the pulmonary artery. The first part of an anomalous subclavian artery can be ligated and cut with impunity, because of the excellent anastomotic blood supply to the arm. In other cases, such as aberrant innominate artery, where it is inadvisable to cut off the blood supply, the offending vessel may instead be displaced and attached in some position where it no longer exerts pressure.

#### TYPES OF ANOMALIES

Though the possible anomalies are innumerable they fall into three main groups, according to the configuration of the aortic arch. The basic embryological pattern is the double aortic arch, from which right and left arches are derived.

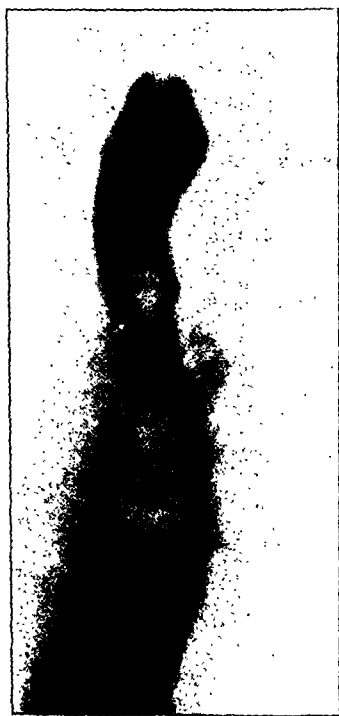


FIG. 1 (Case 1).—S. B., infant girl. Vascular ring, type undetermined.

Symptoms: stridor and attacks of bronchitis, severe vomiting and failure to gain weight. Operation not warranted because of eventual improvement. Radiograph shows bilateral compression of œsophagus containing barium; the trachea was slightly indented and displaced at the same level.

(1) Adrenal Hyperplasia in the Newborn (Inter-renal syndrome), (2) Lung from Infant showing Pneumonia Due to Inhaled Liquor Amnii.—R. AIDIN, M.D.

Developmental Abnormalities of the Teeth in Children.—A. I. DARLING, M.D.S.

Passage of Particulate Matter from Cranial Sub-arachnoid Space to the Nose (see *Arch. Dis. Child.*, 1949, 24, 117).—E. J. FIELD, M.D., J. B. BRIERLEY, M.D., and J. M. YOFFEY, M.D.

The Fetal Kidney.—J. S. BAXTER, M.D.

The Effect of Anæsthetic Drugs on the Suprarenal Cortex.—FRANCES B. ROBINSON, M.B.  
Jenner Bi-Centenary. His original Manuscripts on Vaccination.—A. V. NEALE, M.D.

## Congenital Anomalies of the Aortic Arch and Its Branches

By JOHN APLEY, M.D.

As long ago as 1789 Bayford wrote a fascinating account of a woman, with a life-long history of severe dysphagia, who "fancied that she nourished within her a voracious animal, and attributed all her uneasiness to the fury with which this half-starved monster fell upon each morsel in its passage to the stomach." When, at the age of 62, "worn out with fatigue and famine she sunk into the grave," he carried out a post-mortem examination and published his delightful description with drawings of an anomalous subclavian artery. Bayford's term *dysphagia lusoria* (from *lusus Naturae*—a freak of nature) is still employed, though it is sometimes loosely applied to dysphagia resulting from the many other vascular anomalies which are now recognized. In 1899 Holzapfel collected 200 examples of anomalous right subclavian artery from dissection specimens, but these and similar aberrations were considered as little more than anatomical curios, disregarded in the field of practical medicine.

Congenital anomalies of the aortic arch and its branches produce recognizable effects largely through distortion of the œsophagus and trachea. Diagnosis could, therefore, hardly be expected to progress until radiology contributed its essential quota. The studies of Evans (1936) on the œsophagus, and of Fray (1936) and of Bedford and Parkinson (1936) on right-sided aorta, laid the foundations of radiological diagnosis, now advanced to a high degree of precision in the hands of such exponents as Neuhauser (1946) and other workers. Surgical treatment has advanced concurrently, through the skilful technical innovations of Gross (1947) and others, and the prospect of cure acts as a stimulus to still further progress in diagnosis. Nevertheless, the existence and significance of these anomalies are perhaps still insufficiently appreciated in practice.

### CLINICAL MANIFESTATIONS

In the large majority of cases vascular anomalies produce no recognizable effects. Where signs and symptoms do occur they are suggestive but not pathognomonic, since they are common also to other abnormalities. It is important to realize that the symptomatology varies with age, rather than with the exact type and site of the anomalous vessel. In infancy especially, both the trachea and œsophagus may be distorted, even though the anomalous vessel is in direct contact with only one of these structures. In later life the effects tend to be more localized.

*Respiratory disturbances.*—In infants respiratory disturbances usually predominate. Stridor is the commonest, and usually the sole manifestation, occurring soon after birth. It tends to be aggravated during feeding, and the infant may have to rest frequently while feeding in order to breathe. Often the head is held in the position of hyperextension, apparently to make breathing easier. Inspiratory recession of the ribs and the supra-sternal notch is sometimes very obvious. Chronic or recurrent cough may develop. The increased liability to respiratory infection, due partly to tracheal compression and partly to inhalation of regurgitated food, may lead to permanent lung damage or even prove fatal.

The manifestations described are commonly attributed to "congenital laryngeal stridor", but a search for vascular anomalies is worth while whenever this diagnosis is considered. The diagnosis of "thymic enlargement" may also be made, a misdiagnosis which is all the more plausible because radiological widening of the upper mediastinal shadow, simulating an enlarged thymus, is seen with some vascular anomalies.

*Alimentary disturbances.*—Difficulties in swallowing are generally overshadowed by respiratory difficulties in early life, though later they may come to predominate, and occasionally they occur alone. There may be discomfort on swallowing, or, more frequently, slowness in feeding or refusal to take more than a small amount of food at a time. Irregular vomiting is not uncommon; occasionally vomiting is severe enough to impair nutrition and

vascular ring in conjunction with the pulmonary artery and ductus arteriosus (or ligamentum arteriosum); by direct pressure from a large aortic diverticulum; or by pressure of one of the large aortic branches as it crosses the mid-line (e.g. left common carotid artery). These variants may be recognized by their characteristic radiological features, for which reference should be made to the outstanding paper by Neuhauser (1946).



FIG. 3



FIG. 4

FIG. 3 (Case III).—B. J., girl aged 1 year. *Anomalous innominate artery.*

Symptoms: stridor and persistent cough, repeated lung infection, occasional vomiting, not gaining well. The symptoms improved at 10 months and were lost by the age of 1 year. Angiogram shows innominate artery arising on left side of trachea and crossing to right. Fluoroscopy showed persistent narrowing of œsophagus and trachea at corresponding level.

FIG. 4 (Case IV, by courtesy of Professor C. Bruce Perry).—W. C., boy 5 years old. *Coarctation of aorta.*

No symptoms: investigated because of cardiac murmur. Femoral pulses absent, blood-pressure in arms elevated, heart enlarged. Oblique radiograph with barium in œsophagus shows characteristic "double-C" impression, at an unusually early age.

(3) *Left Aortic Arch.*—In this, the normal mammalian pattern, disturbances may be produced either by abnormalities of the aorta itself or because of the anomalous origin of one of its main branches.

*Abnormalities of the aorta:* Surprising variations occur in the position of the left-sided aorta, even in healthy childhood; a study of these variations is being attempted at the present time. In the presence of certain congenital malformations, such as truncus arteriosus, compression of the œsophagus may be demonstrated radiologically, though it is doubtful whether it produces symptoms. In coarctation of the aorta a similar compression is recognized, and is illustrated in fig. 4. This compression, best seen in the left oblique position, may be in the form of a double C. The upper curve is undoubtedly produced by dilatation of the aorta above the coarctation; the lower curve can sometimes be clearly separated from the impression produced by the left bronchus, and may be due to aortic dilatation below the coarcted area. Other features of coarctation are well known and will not be described.

*Anomalous origin of main branches:* A number of these fascinating anomalies is described in textbooks of anatomy (Gray's Anatomy, 1938), but only a few have been encountered

(1) *Double Aortic Arch*.—This rare anomaly in Man reproduces the vascular pattern normally present in reptiles. The ascending aorta divides and, as a rule, the two limbs encompass both the trachea and œsophagus. If the vascular ring formed in this way is sufficiently small the resulting compression of these structures produces interference with respiration and swallowing. Part of one limb may be represented only by a vestigial cord,

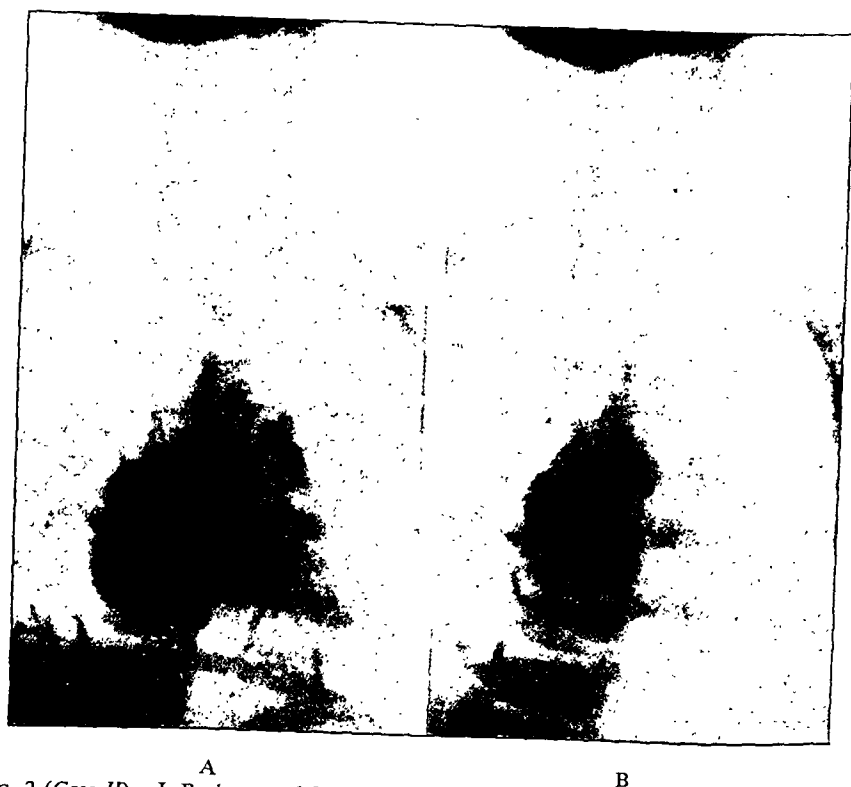


FIG. 2 (Case II).—J. B., boy aged 3 years. *Anomalous R. subclavian artery.*

Probably passing between œsophagus and trachea. Symptoms: stridor decreasing since birth, repeated lung infection, dysphagia and vomiting while weaning. Angiogram A shows anomalous vessel crossing mid-line obliquely upwards and to right (no longer visible in second film B, taken one second later). Earlier investigation when symptoms were severe would probably have shown more marked defects; at 3 years the œsophagus appeared normal and the trachea showed a slight posterior indentation at the level of the anomalous subclavian artery.

but more commonly both limbs remain patent. In such cases the anterior, or left limb is nearly always the smaller and less functionally significant of the two, a circumstance which is fortunate from the surgeon's point of view.

The anomaly is readily diagnosable by demonstrating compression of the œsophagus and trachea; the trachea tends to be compressed from both sides, and the œsophagus posteriorly in addition.

In a series of 7 cases without operation, death occurred in each instance from pulmonary infection (Wolman, 1939). Milder cases undoubtedly occur, with no functional interference or with spontaneous recovery, but in severe cases symptoms have been dramatically abolished by operation (Gross, 1947).

(2) *Right Aortic Arch*.—This anomaly, which is relatively common, reproduces the normal vascular pattern seen in birds. Its occurrence with dextrocardia will not be discussed, since this association merely mirrors the normal, left-sided arch. In the absence of dextrocardia, the common variety of right aortic arch is the posterior type, where the aorta crosses the mid-line towards the left side by passing behind the œsophagus.

In the very small proportion of cases where interference with function occurs it does so through one of four mechanisms: by direct pressure of the aortic arch on the posterior wall of the œsophagus, especially if the vessel is dilated or thickened; by the formation of a

## Section of Radiology

President—J. S. FULTON, C.B.E., T.D., M.D., F.R.C.P.Ed., F.F.R.

[February 18, 1949]

COMBINED MEETING WITH THE BRITISH INSTITUTE OF RADIOLOGY AND THE FACULTY  
OF RADIOLOGISTS

### DISCUSSION ON THE PHYSICAL, CYTOLOGICAL AND MEDICAL ASPECTS OF PROTECTION FROM IONIZING RADIATIONS WITH SPECIAL REFERENCE TO THE USE OF HIGH VOLTAGE X-RAYS AND RADIO-ISOTOPES

Katharine Williams, B.Sc., M.B., M.R.C.P., D.I.H., *Principal Medical Officer,  
Atomic Energy Research Establ., Harwell: Practical Aspects of Medical  
Supervision.*

The principles of protective measures laid down by Sir Thomas Legge (1934) are now widely accepted. The primary responsibility for protection lies with the people who plan the work. Built-in shielding, total or partial enclosure of processes, ventilating systems with general or local exhaust are examples of the type of protection, external to the worker and over which he can exercise no control, which Legge regarded as being of primary importance. The recent rapid progress in nuclear physics with the development of piles, cyclotrons, betatrons and other high energy generators, together with the increasing availability of radioactive isotopes, increased the potential hazards to health from radiations and radioactive substances, including active dusts and gases. Protective measures must keep in step with the new developments. For high voltage X-rays or other high energy radiation the protective measures differ quantitatively rather than qualitatively from those with less powerful machines. Distance and shielding are the two most important factors. The extremely small amounts of radioactive dust and gases which are permissible in the air of a room call for ventilating systems of high efficiency.

Examples of protective measures which, according to Legge, are only partially

clinically, if patent ductus arteriosus be excluded, as is done here. The literature on the clinical side of the subject is extremely recent, and is almost confined to anomalous subclavian artery.

A case of *aberrant innominate artery* has previously been described (Gross and Neuhauser, 1948), and fig. 3 illustrates an additional case. It is interesting to note that in both instances respiratory disturbances were accompanied by vomiting, although the aberrant vessel was in direct contact only with the trachea. *Congenital misplacement of a carotid artery* may also produce symptoms, and this anomaly has been described in a few cases.

*Anomalous right subclavian artery*, on the contrary, is common; its incidence is said to be 16 in every 1,000 autopsies (Goldbloom, 1922). Fig. 2 shows an angiogram of this type of anomaly. In the majority of instances the aberrant vessel passes between the œsophagus and the vertebral column; in a few between the œsophagus and trachea; and rarely its course is anterior to the trachea.

Diagnosis is made by radiological examination of the trachea and œsophagus. Angiography is a luxury which will, however, reveal the anomaly even after the child has grown out of its symptoms (see Case II, fig. 2). The characteristic defect in the barium-filled œsophagus is a narrow indentation, passing obliquely upwards from left to right, at a level immediately above the aortic arch. Its situation on the anterior or posterior aspect of the œsophagus can readily be determined; the rarest type, with the vessel passing anterior to the trachea, has not so far been diagnosed during life.

In only a small proportion of cases do symptoms occur, and operation is rarely indicated. Where it is carried out it may afford immediate relief, with no residual disability.

#### SUMMARY

The clinical significance of anomalies of the aortic arch and its branches is becoming more widely appreciated. Such anomalies are not infrequent, but in the large proportion of cases no untoward effects arise. Where disturbances are produced, however, they may be liable to misinterpretation. In the respiratory tract the commonest are stridor and an increased liability to pulmonary infection. In the alimentary system, difficulties in swallowing and irregular vomiting may occur.

Diagnosis is almost exclusively radiological; the various methods are described, with some illustrative examples. Treatment, apart from chemotherapy of superimposed lung infections, is rarely indicated, because of the tendency to spontaneous recovery, but surgical correction may be life-saving.

A short account is given of various types of anomaly encountered in pædiatric practice.

#### REFERENCES

- BAYFORD, D. (1789) *Mem. Med. Soc. Lond.*, 2, 271.  
 BEDFORD, D. E., and PARKINSON, J. (1936) *Brit. J. Radiol.*, 9, 776.  
 EVANS, W. (1936) *Med. Res. Council, Spec. Rep. Ser.*, No. 208.  
 FRAY, W. W. (1936) *Radiology*, 26, 27.  
 GOLDBLOOM, A. A. (1922) *Surg. Gynec. Obstet.*, 34, 378.  
 Gray's Anatomy (1938) Editor, Johnson, T. B. Longmans Green & Co., Lond. and New York.  
 GROSS, R. E. (1947) *Trans. Stud. Coll. Phys. Philad.*, 15, 43.  
 ———, and NEUHAUSER, E. B. D. (1948) *Amer. J. Dis. Child.*, 75, 570.  
 ———, and WARE, P. F. (1946) *Surg. Gynec. Obstet.*, 83, 435.  
 HOLZAPFEL, G. (1899) see Goldbloom, A. A.  
 NEUHAUSER, E. B. D. (1946) *Amer. J. Roentgenol.*, 56, 1.  
 WOLMAN, I. J. (1939) *J. Pediat.*, 14, 527.

A film of the Bristol Quadruplets was shown, with a commentary by Dr. Beryl Corner.



## Section of Radiology

President—J. S. FULTON, C.B.E., T.D., M.D., F.R.C.P.Ed., F.F.R.

[February 18, 1949]

COMBINED MEETING WITH THE BRITISH INSTITUTE OF RADIOLOGY AND THE FACULTY  
OF RADIOLOGISTS

### DISCUSSION ON THE PHYSICAL, CYTOLOGICAL AND MEDICAL ASPECTS OF PROTECTION FROM IONIZING RADIATIONS WITH SPECIAL REFERENCE TO THE USE OF HIGH VOLTAGE X-RAYS AND RADIO-ISOTOPES

Katharine Williams, B.Sc., M.B., M.R.C.P., D.I.H., *Principal Medical Officer,  
Atomic Energy Research Establ., Harwell: Practical Aspects of Medical  
Supervision.*

The principles of protective measures laid down by Sir Thomas Legge (1934) are now widely accepted. The primary responsibility for protection lies with the people who plan the work. Built-in shielding, total or partial enclosure of processes, ventilating systems with general or local exhaust are examples of the type of protection, external to the worker and over which he can exercise no control, which Legge regarded as being of primary importance. The recent rapid progress in nuclear physics with the development of piles, cyclotrons, betatrons and other high energy generators, together with the increasing availability of radioactive isotopes, increased the potential hazards to health from radiations and radioactive substances, including active dusts and gases. Protective measures must keep in step with the new developments. For high voltage X-rays or other high energy radiation the protective measures differ quantitatively rather than qualitatively from those with less powerful machines. Distance and shielding are the two most important factors. The extremely small amounts of radioactive dust and gases which are permissible in the air of a room call for ventilating systems of high efficiency.

Examples of protective measures which, according to Legge, are only partially  
Nov.—RADIOLOG. 1

successful because they depend on the will or whim of the worker to use them are protective clothing, eyeshields and respirators. Education of the workers in the nature of the health hazards is essential. Physicians charged with their health protection may need to use a great deal of tact and persuasion to enlist the co-operation of staff in their own health safety.

Distance is the best and easiest form of protection: the staff should know the inverse square law for decrease of intensity of gamma rays with distance from the source; the range of beta particles and the rapid decrease with distance of beta radiation. Distance cannot always be used, so shielding is necessary. Even though beta particles of average energies are stopped by a few millimetres of glass—about 3 mm. in the case of radiophosphorus—it is still a good rule to use tongs or forceps with highly beta active solutions. Present-day glassware is often thin and a considerable amount of the radiation will get through, so that handling with bare hands should be avoided. Rubber gloves or paper should be used when handling beta-active materials. Spills on clothing, if allowed to dry and come in contact with skin, may cause injury. Low Beer (1946) has shown that 34 microcuries of radiophosphorus applied to one square centimetre of skin for one hour gives a perceptible erythema. It is not safe to allow a continual skin contamination over long periods of time of more than a few hundred counts per minute of typical beta ray activity.

The gamma radiation from most isotopes will be absorbed by about 2 in. of lead in the majority of cases—though in the more energetic gamma rays, such as those of  $\text{Na}^{24}$ , about 10% would penetrate this shield.

Good housekeeping is essential. Spills are dangerous. Spills of solutions will dry and the active dust will be disseminated through the air of the room on to floors and benches and possibly into adjacent rooms also. A glass vessel must be placed inside a second container or tray. It is a good rule to work inside stainless steel trays, and to keep special trays lined with absorbent paper for tubes, pipettes and stirring rods, and to make it a rule never to place them on the laboratory bench after use (M.R.C., 1949). If the working conditions are bad, a few millicuries may be potentially more harmful than 1,000 curies under proper working conditions.

To limit airborne activity, experiments with dry materials, or those giving off gases or vapour, should be carried out in an airtight dry box or in a fume cupboard. Dust must not be allowed to collect, and walls, floors, benches must be easy to clean and free from cracks or crevices where dust can lodge. Waxed linoleum is a good floor covering, walls should be plastered and coated with a hard gloss or strippable paint. Laboratory benches and fume cupboards should be made of or covered with glass or stainless steel. A wooden laboratory bench is liable to absorb radioactivity in case of a spill—if wood is used, painting with a hard gloss paint is advisable. Protective clothing, including gloves, coveralls or laboratory coats and possibly a change of shoes should be provided and worn, with rooms for washing and changing. The scrupulous care, cleanliness and discipline of a bacteriological laboratory should be observed.

Constant checking of conditions is essential, and a small portable monitoring instrument should always be at hand. Unsuspected leakage and scattered radiation may be hazardous. It is not safe to assume that a bench or table-top affords sufficient protection. A thin brick wall or a partition, floor or ceiling may not be sufficient protection for the unsuspecting occupants of contiguous rooms: there are six sides to a room. The monitoring should be continual: unsuspected leakages in shielding scattered radiation will only be detected if this is done. Area monitoring must also include estimations of the amount of active dusts and gases in the air of the rooms.

The maintenance of the health of the workers is the final and acid test of the efficiency of the planning procedures and working conditions. But the results cannot

be given either quickly or easily. It is essential to attempt to detect radiation damage as quickly as possible and to prevent further damage from occurring. Any clinical test should give reliable information about the individual, but this means assessing individual radiosensitivity. It is not uncommon for doses varying by a factor of 2, even up to a factor of 5, to produce a given biological effect in different individuals. Clinically the normal base line of the health of each individual worker must be established, so that any significant deviation from this base line can be noted. The quantitative measure of occupational exposure is helpful in assessing the probability of occupational exposure as the causative factor of deviation from normal.

A pre-employment or pre-exposure medical examination is of importance in establishing the normal of the individual. This includes a full history, personal and occupational; history of previous radiation exposure, including screening for diagnostic purposes; clinical examination; blood-count and X-ray of chest. Condition of skin, nails and eyes should be noted. This is followed by routine follow-up examinations during exposure.

Examination of the circulating blood has long been recognized to be of value in the clinical assessment of occupational over-exposure to radiation. Characteristic changes in blood-counts occur frequently but individual variation is very great. As an indication of early damage, the blood-count is one of the fairly satisfactory types of evidence, but it is becoming increasingly evident that the classical hæmatological methods are not sufficiently sensitive. It is recommended that a base line should be established by taking two or three counts several days apart before exposure, at the same time of day (to exclude diurnal variation). Other possible factors influencing the count should be noted, including chemical laboratory reagents such as benzene and the sulphonamide and amidopyrine drugs used therapeutically.

Most previous work has been devoted to changes in the numbers of cells of different types. Although immediately after therapeutic radium implantation or surface application there is frequently a rise in the absolute number of neutrophil leucocytes in the circulating blood, the lymphocytes usually show a rapid and progressive decrease in numbers. With occupational over-exposure, there is frequently leucopenia due to neutropenia and certain individuals exhibit an absolute lymphocytosis. Jacobson (1947) considers a lymphopenia the most sensitive indication of radiation damage. Goodfellow (1935) has shown that "the appearance of embryonic white cells in the blood has coincided with such occasions of excessive exposure which leaves no doubt, if indeed there could be any, that irradiations were responsible for such definite departures from the normal". "In the majority of instances the abnormal cells observed have been Türk cells." "On several occasions other forms of atypical lymphocytes were seen. These were more normal in general appearance, but the cytoplasm contained minute eosinophilic granules. Less frequently monocytes exhibiting similar changes have made their appearance at times when the individuals concerned had a low white cell count" (1936).

Dickie and Hempelmann (1947) have described also a greater increase in the number of abnormal leucocytes containing neutral red bodies, demonstrated by a supravital technique, in workers exposed to radiation in the tolerance range than in workers exposed to chemical toxins. Nearly all the individuals exposed to gamma rays of less than 0.1 r/day had more than 20%, but only about one-third of the individuals exposed to chemical toxins had more than 20%. Browning (1949) has found large abnormal monocytes with pyknotic nucleus and granular cytoplasm in luminizers—these disappear from the blood picture after a period of non-exposure.

Dickie and Hempelmann (1947) have shown that the mean leucocyte count of a group of individuals exposed to a daily dose of radiation of probably less than 0.1 r was lower than that of a similar group of normal unexposed persons. Such a finding

should focus attention on the working environment of such a group and statistical comparison has been recommended as a reasonably accurate diagnostic procedure (Cronkite, 1949).

At present we do not know what significance to attach to these findings. It is not easy to decide at what point it is prudent to advise that any particular individual should cease to have exposure temporarily or permanently. A study of cytological abnormalities of the leucocytes of the circulating blood using the quantitative method of ultraviolet photomicrography, by which, in a series of papers (1940, 1942, 1943 and 1944), Mitchell has demonstrated disturbances of the cellular nucleic-acid metabolism, offers a promising avenue of approach.

Laboratory tests by biochemical and counting methods form an essential part of the clinical investigations. Essentially these are tests of excretion of internally deposited radioactive materials. With radioactive isotopes we are not as fortunate as in the case of radium and radon which have certain physical and radioactive properties which can be used for testing internal deposition: radon in breath, and Ra as RaC can be detected by external gamma radiation. With radio-iodine the localized emission from the thyroid gland can be measured, but only very rarely can general gamma emission be used: it would be possible with Na<sup>24</sup>. So, in general, the method used is to concentrate the radioactive material from urine—preferably a twenty-four-hour specimen—and estimate the amount present. With uranium we use the property that, fused with sodium fluoride, fluoresces in ultraviolet light (Stone, 1946). The method is sensitive—in our workers, the excretion is less than 5 microgrammes per litre of urine.

Beta counting (by Geiger-Müller counters or ionization chambers) is used for the more generally available isotopes. In general, it will be advisable to make some separation from inert matter.

The aim is to estimate the amount retained in the body, and it is possible to make a fairly reasonable guess. But as our assumptions on the rate of excretion are based on the results of animal experiments, the results are not precise quantitative values. We are specially concerned to determine whether any slow accumulation of repeated small doses is taking place, in particular, with long-lived radioactive materials believed to have a low excretion. The method is also used to get as good a figure as possible for the intake in an accidental happening.

When radioactive isotopes become more generally available and are used in hospitals for research purposes or as therapeutic agents, protective measures of greater or lesser extent will be needed. It may be advisable to consider possible hazards to the nursing and technical staff who will handle the urine and stools in which the radioactive material is excreted: and even potential hazards to the occupants of adjacent beds. Random handling throughout the hospital is likely to lead to a spread of contamination. Probably it would be an advantage to have a special reception or preparation room where radioactive isotopes could be received and prepared for administration; special storage space for sources; equipment, glassware and syringes used for radio-isotopes specially marked and not used elsewhere in the hospital. Howarth (1948) considers isotope work to be totally unsuited to the general clinical laboratory of a hospital.

Adsorption of active material on glass is not uncommon, so, even after washing, the glassware should not be mixed with new items and should be segregated after use. Possibly it will be found an advantage to set aside a separate room or wing of the building for therapy with radioactive isotopes. The laboratory staff concerned in the preparation of injections and estimations of amounts excreted must be trained to observe the necessary precautions and should be under medical supervision.

Attention has been drawn to the risks of radioactive isotopes (*Brit. med. J.*, 1947) and Mitchell (1947) and Howarth (1948) have stated the need for caution. It is important to avoid the possible danger of carcinogenesis which might result from the introduction of radioactive materials, including  $P^{32}$  and  $I^{131}$ , into the body and also the possible effect on spermatogenesis and oogenesis in young persons (McWhirter, 1947). The conclusion is drawn that in the present state of knowledge it is in general unwise to use  $P^{32}$  to treat patients who are in the reproductive period of life or who have an expectation of life of five years or more (*Brit. med. J.*, 1947).

Provided suitable protective measures are taken in handling radioactive isotopes and discretion is exercised in their use for therapeutic purposes, safe conditions can be achieved. At Harwell it has been possible to keep the average weekly exposure of staff working with ionizing radiation or radioactive substances to less than 1/10 of a roentgen a week since the Establishment began. No ill-effects on health have been observed.

#### REFERENCES

- Brit. med. J.* (1947) (ii), 778.  
 BROWNING, E. (1949) *Brit. med. J.* (i), 428.  
 CRONKITE, E. P. (1949) *J. Amer. med. Ass.*, 139, 366.  
 DICKIE, A., and HEMPELMANN, L. H. (1947) *J. Lab. clin. Med.*, 32, 9.  
 GOODFELLOW, D. R. (1935) *Brit. J. Radiol.*, 8, 669.  
 — (1936) *Acta radiol. Stockh.*, 17, 1.  
 HOWARTH, F. (1948) *Lancet* (ii), 41.  
 JACOBSON, L. O., and MARKS, E. (1947) *Radiology*, 49, 286.  
 LEGGE, T. (1934) *Industrial Maladies*. Oxford.  
 LOW BEER, B. V. A. (1946) *Radiology*, 47, 213.  
 MCWHIRTER, R. (1947) *Brit. med. J.* (ii), 783.  
 MITCHELL, J. S. (1940) *Nature*, 146, 272.  
 — (1942) *Brit. J. exp. Path.*, 23, 285, 296, 309.  
 — (1943) *Brit. J. Radiol.*, 16, 339.  
 — (1944) *Amer. Rep. Brit. Emp. Cancer Campaign*, 62.  
 — (1947) *Brit. J. Cancer*, 1, 1.  
 Introductory Manual on the Control of Health Hazards from Radioactive Materials. *Med. Res. Counc. Issue No. 2*, 38, Old Queen St., S.W.1. Jan. 1949.  
 STONE, R. S. (1946) *Proc. Amer. phil. Soc.*, 90, 11.

W. G. Marley, M.Sc., Ph.D., *Atomic Energy Research Establishment, Harwell: Physical Methods of Achieving Protection for High Energy Radiation and Radioactive Isotopes.*

#### INTRODUCTION

Almost immediately following the actual discoveries of X-rays and of the naturally occurring radioactive isotopes, instances occurred of radiation injury and it was very quickly obvious that protective measures would have to be adopted in the development and application of these discoveries. In the early work the measures were largely corrective and were applied following the instances of over-exposure, but nowadays sufficient is known for precautions to be taken in advance and the methods are accordingly preventative. The large increase in the use of radioactive materials and of radiotherapy has led to considerable numbers of persons being exposed to radiation hazard and has necessitated the development of the special branch of applied physics known as Health Physics. A further reason for this has been the necessity, in the development of atomic energy, of carrying out work with radioactive materials on a factory scale where large numbers of non-professional persons are exposed to radiation hazards: in these circumstances a considerable organization is necessary which, on the research scale, can usually be dispensed with.

#### GENERAL NATURE OF HAZARDS AND THE BASIS OF PROTECTION

It is generally believed that the hazard from inhalation and ingestion of radioactive materials is much more serious than that from external radiation, largely

because of the difficulty of knowing when exposure has occurred and when material has, in fact, been taken into the body. The further hazards which arise from the various kinds of external radiation include, in a large institution such as the Atomic Energy Research Establishment at Harwell, not only alpha, beta and gamma rays from radioactive materials but also hard gamma rays and neutrons of various energies produced by the piles, Van der Graaf generators and the large cyclotron.

Protection is normally achieved by defining a permissible maximum exposure or tolerance for a particular kind of radiation or for a given radioactive isotope, as a result of specific animal experiments or from the effect upon human beings of high doses of radiation in radiotherapy work or from accidental exposure to high doses; a particular instance of the latter is the series of cases of accidental over-exposure during the first World War which has yielded such valuable information in relation to the radium tolerance for human beings. When a tolerance has been defined it is generally possible to assess the hazard by measurement of some physical quantity such as the intensity of the radiation or the concentration of the radioactive isotope.

In order to ensure protection it is thus necessary to measure the radiobiological dose experienced by personnel due to external beta and gamma rays and neutrons of all energies: measurements have also to be made of the activity of radioactive dust which might get into the air. It is also necessary to arrange for effective control of hazards from the disposal of radioactive waste materials and from local accumulations of active gases and dust. Hazard control also involves the proper design of laboratories and plant to avoid persistent contamination and exposure, and the preparation of protection manuals and the necessary education of new staff. If the dosage experienced is to be kept down, considerable attention must be paid to the proper design of shields for apparatus containing radioactive sources and also for any high energy machines. Appropriate values for necessary shielding for beta radiation and for gamma radiation and the detailed protection procedure may be obtained by reference to the two manuals which have been made available by the Medical Research Council, namely the "Recommendations of the British X-ray and Radium Protection Committee" and the "Introductory Manual for the Control of Health Hazards from Radioactive Materials."

In any laboratory where high energy radiation or radioactive isotopes are used, it is desirable that one person, usually a physicist, should be made responsible for all protection arrangements and that he should work in close collaboration with a qualified medical adviser. The Health Supervisor should be responsible for drawing up rules and regulations relating to the conduct of work and also for organizing the monitoring and other protection procedures outlined above. The Health Supervisor should also arrange for regular blood counts to be taken for all persons likely to be exposed to radiation and for an analysis of the results by a pathologist acquainted with the hæmatological effects of exposure to radiation [1]. Arrangements should also be made for periodical medical examination of all staff involved and, in particular, that their hands are frequently examined by an expert.

It will be seen that adequate radiation hazard control of a large establishment involves a wide range of technology and an extensive organization. Precautions in this work are expensive, but perhaps not nearly so expensive as the consequences of failure.

#### THE MAXIMUM PERMISSIBLE (TOLERANCE) DOSE

Consideration will now be given to the evaluation of the maximum permissible dose of radiation and of exposure to radioactive isotopes which can be continued indefinitely without discernible effect on the body.

*External radiation.*—In 1931, a League of Nations publication by Wintz and Rump [2] concluded that the permissible exposure was  $10^{-5}$  roentgen/second, assuming a

seven-hour working day and 300 working days per year. This is equivalent to 0.25 roentgen/day, but for persons exposed to non-intermittent sources the report recommended that the figure should be reduced by a factor of 3. The figure of 0.2 roentgen/day was subsequently adopted by the International Committee on X-ray and Radium Protection and still remains in the International recommendations [3]; the limit of 0.1 roentgen/day has, however, become widely established in atomic energy establishments during the war. After reviewing the results of a wide range of biological experiments and experience with X-rays and gamma rays, the Protection Sub-Committee of the British Medical Research Council recommended [4] in 1948 the adoption of 0.5 roentgen/week as the maximum permissible exposure to X or gamma radiation which may be continued over an indefinite period. In work with radioactive isotopes, no tissue or organ of the body should accordingly receive more than this or the equivalent quantity, 0.5 rep<sup>1</sup>, of beta radiation, in one week, except for the hands which may receive up to 1.5 rep per week. It is, however, advisable [5, 6] to strive for the lowest possible exposure in every operation and the average exposure should be kept well below the limiting figure.

Whilst the maximum permissible exposure for the beta and gamma rays from radioactive isotopes is 0.5 rep/week, it has been recommended that the tolerance for alpha particles should be one-tenth of this, to allow for the higher specific ionization along the particle tracks and the increase in damage produced. The mechanism of damage in fast neutron irradiation is complicated by the recoil of protons and by the energy released in the capture of neutrons in nitrogen. In view of numerous experiments and calculations [7, 8] on this subject, it appears that the maximum permissible dose of neutrons received in one week should not exceed about one-twentieth of that for X and gamma rays when measured physically (i.e. in rep).

*Internal radiation.*—A great deal of experimental work has been done during the war upon the effect of inhaled and ingested radioactive isotopes upon animals and it appears that the most dangerous isotopes are probably those which, like radium, are deposited in the skeleton [9]. As a result of considerable experience with radium poisoning in man, it is now generally agreed that for persons subject to monitoring control the maximum permissible body burden of radium is 0.1 microgram. By means of animal experiments, Brues [10] has determined the relative toxicity of Sr<sup>90</sup> and Ra from which it appears that the maximum permissible human body burden of Sr<sup>90</sup> is probably about 1 microcurie. From these basic data, it is possible to compute tolerances for a number of similar isotopes and equivalent quantities for other isotopes can be computed in a similar way, taking into account the nature of the radiation and the metabolic processes, such as absorption, excretion, location and translocation in the body.

#### THE MEASUREMENT OF RADIATION INTENSITY AND DOSAGE

Once a tolerance has been defined for a given type of radiation or radioactive isotope, protection depends upon measurement of the dose-rate for the radiation or of the concentration of the isotope, and it is essential that sufficient and suitable instruments are provided for this purpose. A wide range of measuring instruments is now commercially available for personnel monitoring, area monitoring, dose-integration and a number of ancillary purposes such as the measurement of the contamination on the hands or the pollution of the air of the laboratory with radio-

<sup>1</sup>The roentgen-equivalent physical (rep), introduced by H. M. Parker, is the radiological dose produced in tissue by radiation other than X-rays or gamma rays, which produces the same energy absorption in tissue as 1 roentgen of X-rays or gamma rays. The energy absorption for 1 roentgen of X-rays or gamma rays is 83.8 erg/g. of air or 93.1 erg/g. of water. Since tissue and water have very similar characteristics in this respect, a dose of 1 rep thus corresponds to an energy absorption of 93.1 erg/g. in tissue.

because of the difficulty of knowing when exposure has occurred and when material has, in fact, been taken into the body. The further hazards which arise from the various kinds of external radiation include, in a large institution such as the Atomic Energy Research Establishment at Harwell, not only alpha, beta and gamma rays from radioactive materials but also hard gamma rays and neutrons of various energies produced by the piles, Van der Graaf generators and the large cyclotron.

Protection is normally achieved by defining a permissible maximum exposure or tolerance for a particular kind of radiation or for a given radioactive isotope, as a result of specific animal experiments or from the effect upon human beings of high doses of radiation in radiotherapy work or from accidental exposure to high doses; a particular instance of the latter is the series of cases of accidental over-exposure during the first World War which has yielded such valuable information in relation to the radium tolerance for human beings. When a tolerance has been defined it is generally possible to assess the hazard by measurement of some physical quantity such as the intensity of the radiation or the concentration of the radioactive isotope.

In order to ensure protection it is thus necessary to measure the radiobiological dose experienced by personnel due to external beta and gamma rays and neutrons of all energies: measurements have also to be made of the activity of radioactive dust which might get into the air. It is also necessary to arrange for effective control of hazards from the disposal of radioactive waste materials and from local accumulations of active gases and dust. Hazard control also involves the proper design of laboratories and plant to avoid persistent contamination and exposure, and the preparation of protection manuals and the necessary education of new staff. If the dosage experienced is to be kept down, considerable attention must be paid to the proper design of shields for apparatus containing radioactive sources and also for any high energy machines. Appropriate values for necessary shielding for beta radiation and for gamma radiation and the detailed protection procedure may be obtained by reference to the two manuals which have been made available by the Medical Research Council, namely the "Recommendations of the British X-ray and Radium Protection Committee" and the "Introductory Manual for the Control of Health Hazards from Radioactive Materials."

In any laboratory where high energy radiation or radioactive isotopes are used, it is desirable that one person, usually a physicist, should be made responsible for all protection arrangements and that he should work in close collaboration with a qualified medical adviser. The Health Supervisor should be responsible for drawing up rules and regulations relating to the conduct of work and also for organizing the monitoring and other protection procedures outlined above. The Health Supervisor should also arrange for regular blood counts to be taken for all persons likely to be exposed to radiation and for an analysis of the results by a pathologist acquainted with the hæmatological effects of exposure to radiation [1]. Arrangements should also be made for periodical medical examination of all staff involved and, in particular, that their hands are frequently examined by an expert.

It will be seen that adequate radiation hazard control of a large establishment involves a wide range of technology and an extensive organization. Precautions in this work are expensive, but perhaps not nearly so expensive as the consequences of failure.

#### THE MAXIMUM PERMISSIBLE (TOLERANCE) DOSE

Consideration will now be given to the evaluation of the maximum permissible dose of radiation and of exposure to radioactive isotopes which can be continued indefinitely without discernible effect on the body.

*External radiation.*—In 1931, a League of Nations publication by Wintz and Rump [2] concluded that the permissible exposure was  $10^{-5}$  roentgen/second, assuming a



activity handled are in the region of millicuries or greater, to have portable electronic dose-rate meters and a convenient instrument of this type is shown in fig. 2. Mains operated monitors mounted on the bench and provided with a probe incorporating a Geiger-Müller counter are also exceedingly convenient for the control of contamination in the laboratory and a model used at Harwell is shown in fig. 3: it has two probes,



*Crown copyright reserved.*

FIG. 2.—Pistol-grip type of ionization chamber electronic dose-rate meter.

one (in the clip on top) for beta-gamma measurement and the other (on the bench in front) for alpha measurements. It should be noted, however, that Geiger counters have some limitation when used for the measurement of dose-rate and for this purpose ionization chambers are to be preferred. In laboratories where work is carried out continuously with radioactive material, it is also convenient to have an integrating dose-meter which measures the total dose received since the beginning of operations on any given day and indicates this on a clearly read dial in the laboratory. Such an instrument can frequently be provided with an alarm if the dose-rate becomes very high or if the total dose received since the beginning of the day rises above a certain specified value. Further details of the area instruments mentioned are being published [11] and particulars of their commercial availability may be obtained from A.E.R.E., Harwell.

A further aspect of area monitoring is the measurement of neutron fluxes in the vicinity of piles, cyclotrons, and Van der Graaf generators. It is necessary to distinguish between fast neutrons and slow neutrons, the fluxes of the former being measured by ionization produced by the recoil of protons in a high-pressure hydrogen-filled ionization chamber, and the latter by an ionization measurement in a chamber filled with boron trifluoride. Since fast neutron fluxes are usually associated with an appreciable gamma-ray background, it is usually necessary to compensate for the ionization produced by the gamma-rays by taking subsidiary measurements with a

active dusts, but the measurement of fast neutron intensities in the presence of gamma rays still involves complicated physical measurements and simple equipment has not yet been devised.

*Personnel monitoring.*—The film badge containing a small piece of X-ray film, part covered by 1 mm. of lead, forms a convenient permanent record of the exposure of a given individual to X, beta and gamma radiation, and should be considered as an essential requirement in every institution: an appropriate film-badge service is available from the National Physical Laboratory, Teddington. It is now possible also to use film badges for the measurement of the dosage from slow neutrons by the use of loaded emulsions containing lithium or boron, whilst fast neutrons can also be estimated from the hydrogen recoils in suitable emulsions, the estimation in these instances being made by track counting. Persons engaged with appreciable quantities (say millicuries of radioactive material) or who are moving around in areas where the radiation dose-rate is not readily predictable should carry pocket ionization chambers which can be quickly read and give an immediate indication of the gamma-ray dose received in any given operation.

Apparatus should also be provided in all laboratories where active material is manipulated so that persons can check their degree of personal contamination at the conclusion of any given operation. It is customary in atomic energy plants such as Harwell to provide hand, foot and clothing monitors in the wash rooms associated with active laboratories. Fig. 1 shows such an instrument being used to check con-

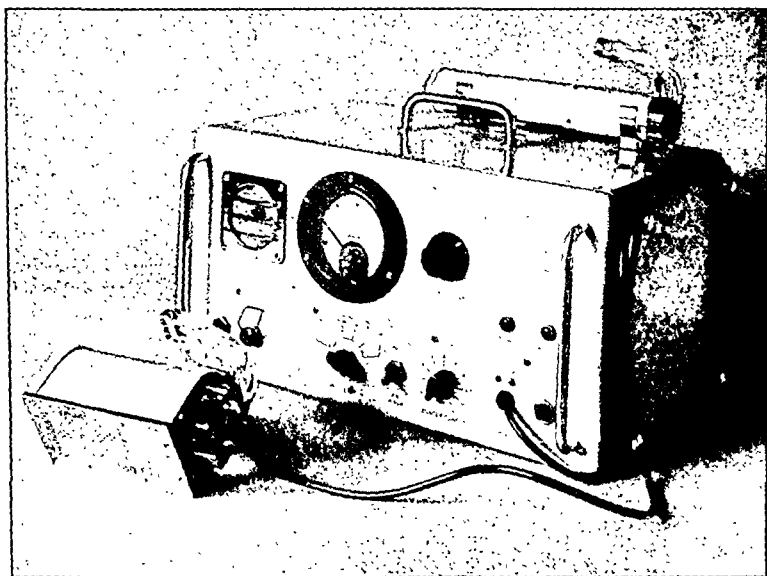


*Crown copyright reserved.*

FIG. 1.—Clothing contamination being checked by clothing probe of hands, feet and clothing monitor.

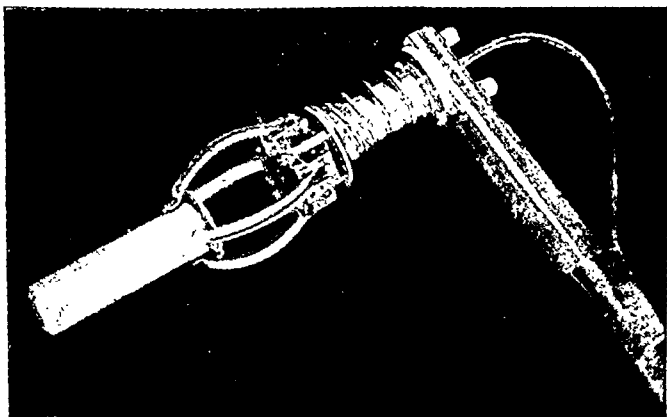
tamination on an overall. Simple instruments can often be devised for this purpose in a small laboratory by the use of a Geiger-Müller counter probe monitor.

*Area monitoring.*—For the purpose of the control of radiation intensities in areas where radioactive materials are manipulated, it is essential, when the quantities of



*Crown copyright reserved.*

FIG. 3.—Mains operated contamination monitor with beta probe (in clip on top) and alpha probe (on bench in front).



*Crown copyright reserved.*

FIG. 4.—Remote-operated grab for safe handling of isotope containers on removal from the pile.

#### DISPOSAL OF ACTIVE WASTE

In order to prevent hazards arising from the accumulation of activities in waste systems and to safeguard drinking water supplies, great care is necessary in the disposal of radioactive wastes. As far as possible active material should be precipitated from solution and disposed of as an insoluble residue. Small quantities of beta-gamma isotopes may, however, be disposed of in alkaline solution by washing down a normal sewage system; the quantities which may be disposed of in this way are, however, very strictly limited and reference is made to these in the M.R.C. Manual on the handling of radioactive materials to which reference is made above. The Manual also indicates the procedure for disposal of contaminated glass and

similar ionization chamber filled with argon. Where the measurements have to be extended up to energies of the order of 200 MeV, very great difficulties are encountered and a completely satisfactory method of measurement has not yet been developed.

*Air-contamination monitoring.*—Many beta- and alpha-active isotopes, especially those which are selectively deposited in a particular organ, such as the skeleton [9], can give rise to a considerable hazard through ingestion or inhalation and this must be guarded against by the use of efficient hoods and by systematic monitoring of the air for active dust and aerosols. Monitoring is normally carried out by drawing a considerable volume of air through a filter paper and counting the alpha or beta activity collected, due allowance being made for radon and thoron decay products which will also be collected.

#### SPECIFIC HAZARDS OF PHYSICS AREAS

The more hazardous radiations encountered specifically in physics areas include hard gamma rays, hard X-rays and fast neutrons. In general, these radiations arise from fixed sources, such as piles, cyclotrons or Van der Graaf generators and the radiation experienced is substantially constant and does not vary from day to day; its intensity depends essentially upon the design of the shielding and it is often possible to survey these machines and then to ensure that the circumstances do not change appreciably following the survey. The measurement of radiobiological dose for very high energy neutrons from the cyclotron presents considerable difficulties to which reference has been made above. Recent clinical cases of damage to the eyes of cyclotron workers from excessive fast neutron exposure have focused attention on this particular hazard but there appears to be no reason to make any change in the present fast neutron tolerance [7] as a consequence of these instances involving high exposures.

Neutron hazards also arise from the operation of the piles: it is necessary, for instance, to guard against exposure to neutron beams coming from holes in the pile shield, uncovered for experimental purposes: a rigid operational procedure is necessary and, in addition, a watch is kept on the slow neutron background indicated by the boron trifluoride-filled ionization chambers installed locally.

#### SPECIFIC HAZARDS OF THE CHEMISTRY AREAS

The main problem in chemistry areas is the prevention of contamination of the laboratory benches, fume hoods and floor and also of the air due either to normal operations or as a result of carelessness. The provision of suitable monitors, especially those of the type shown in fig. 3, together with ceaseless vigilance, is essential to prevent the build-up of contamination. Some control can also be effected by limiting the quantities of active material which may be handled in any given laboratory, the amount depending on the design of the laboratory and equipment. The provision of well-designed remote handling devices can generally reduce the dosage very considerably and it is desirable to have one or two people who specialize in the design of quite complicated mechanisms for use in routine operations to avoid the necessity or temptation for the hands to be brought near to the active source. An example of such a piece of equipment is the device shown in fig. 4 for handling isotope containers on removal from the pile. Good design of apparatus can also reduce the exposure experienced in the handling of strong sources, especially of beta-active isotopes where it is often desirable to build the apparatus on the back of a transparent plastic shield with all the taps and controls brought through. In all active chemical laboratories it is essential to wear special laboratory clothing and this should be worn only in the active laboratories. Rubber gloves should always be worn in all operations with open sources of radioactive material.

## Section of United Services

President—Sir HENRY TIDY, K.B.E., M.A., M.D., F.R.C.P.

[December 2, 1948]

### DISCUSSION: POST-GRADUATE MEDICAL EDUCATION IN THE SERVICES<sup>1</sup>

**Sir Henry Tidy, K.B.E., M.D.:** This Section held its last meeting in 1940. It was then deemed advisable that it should be suspended during the War. Its place was taken to some extent by the Inter-Allied Conferences on War Medicine which were convened by the Royal Society of Medicine and held in this House from 1942 to 1945.

The time has now come when the Section can usefully resume its activities. It is not intended immediately to hold regular meetings but to arrange discussions when suitable subjects present themselves.

We have before us a matter of great importance to all three Services and we must trust that the discussion will be of value to the Authorities concerned.

**Surgeon Vice-Admiral Sir Henry Colson, K.C.B.,** *Medical Director-General of the Navy.*

#### *Introductory remarks :*

The question of the post-graduate education of specialists is one of great interest to all in the Services.

The purpose of the Medical Services may be defined as follows :

(1) To act as a cache in peace of Service-trained medical officers, which in the event of war could be rapidly expanded into an efficient Medical Service.

(2) To look after the health of the Service in peacetime, not only to treat the sick but also to prevent disease.

The R.N. Medical Service is called a part-time service as Medical Officers have to do some sea time but this is only for a short period ; on investigation of a sample number of specialists it was found that only about fifteen months was spent at sea in ten years.

It has been found that good specialist officers make good administrators.

**Surgeon Captain J. G. Holmes, O.B.E., M.A., M.D.,** *Royal Navy (formerly Medical Specialist):* (1) It was customary for young medical men on joining the R.N. to have a short course of instruction at a naval hospital—there in addition to the routine work one learned about naval customs, picked up Service jargon, learned something of naval hygiene, visited ships and establishments and so forth. Then followed a commission at sea—maybe on one's own in a gunboat in China—where

<sup>1</sup>The opinions expressed are the authors' own personal views and have received no official authorization.

other solid waste. Animal remains should, in general, be passed through an incinerator in which provision has been made for filtering out any active dust which might arise in the incineration process and the ash from the incinerator should be treated as other radioactive solid waste from the laboratory. With simple precautions of this nature, radioactive work in laboratories can be carried out without danger of the spread of contamination and without hazard arising to the local population.

#### ACKNOWLEDGMENT

Acknowledgment is made to the Director, A.E.R.E., Harwell, for permission to publish this paper and to Dr. D. Taylor for the (hitherto unpublished) photographs of items of monitoring equipment developed in the Electronics Division.

#### REFERENCES

- 1 JACOBSON, L. O., MARKS, E., and LORENZ, E. (1949) Hæmatological effects of ionizing radiations, *Radiology*, **52**, 371.
- 2 WINTZ, H., and RUMP, W. (1931) League of Nations Publ. III, 9 (CH— 1054).
- 3 International recommendations for X-rays and radium protection (1934) *Radiology*, **23**, 682; and (1937) *Radiology*, **30**, 511.
- 4 Introductory Manual on the Control of Health Hazards from Radioactive Materials, Issue No. 2, Jan. 1949, *Med. Res. Council*, 38 Old Queen Street, London, S.W.1.
- 5 HENSHAW, P. S. (1941) Biologic significance of the tolerance dose in X-ray and radium protection, *J. Nat. Cancer Inst.*, **1**, 789.
- 6 SIEVERT, R. M. (1947) The tolerance dose and the prevention of injuries caused by ionizing radiations, *Brit. J. Radiol.*, **20**, 306.
- 7 MITCHELL, J. S. (1947) Provisional calculation of the tolerance flux of fast neutrons, *Brit. J. Radiol.*, **20**, 177.
- 8 — (1947) Experiments on the biological action of fast neutrons, *Brit. J. Radiol.*, **20**, 368.
- 9 HAMILTON, J. G. (1948) Metabolic properties of the fission products and actinide elements, *Rev. Mod. Phys.*, **20**, 718.
- 10 BRUES, A. M., LISCO, H., FINKEL, M. Carcinogenic action of some substances which may be a problem in certain future industries. U.S.A.E.C. Declassified report MDDC 145.
- 11 TAYLOR, D. (1949) Radiation monitoring and surveying apparatus. *Atomics*, Vol. 1 (in the press).

(3) I believe that every specialist should have a good knowledge of the sailor and his working conditions. To obtain this he must go to sea and thus he must have some break in the practice of his speciality at least two or three times in his Service career. We should develop our own consultants (right up through the rank of Surgeon Captain to Surgeon Rear-Admiral) from men who have both the professional ability, the necessary recognized degrees and the broad background of knowledge of the Navy and its personnel (what I may call my three postulates). There may be a case for the surgeon (general, orthopædic, E.N.T., &c.) not having any break in the practice of his technical art—the case for the physician and psychiatrist may not be so rigid or indeed desirable. I have known at least three medical specialists—one now retired, one a contemporary of my own, one still comparatively junior—who would adequately fulfil my three postulates for attaining high rank as consultant physicians to the Navy. And the same applies in other specialities.

**Brigadier D. C. Bowie, O.B.E., F.R.C.S., Consulting Surgeon, M.E.L.F.:** The views expressed in this paper are my own; they are not official, but are based upon some thirty years' experience as an army surgeon and pointed by recent experience as Reader in Military Surgery at the Royal Army Medical College. At the outset it is in my view beyond question that a suitable proportion of regular officers must be trained as specialists in the Army Medical Service. Unless this is permitted, the R.A.M.C. will speedily become defunct as a body of professional medical men.

The army specialist surgeon must have the same training, the same higher qualifications and therefore the same status as his colleague of specialist standing in civil life. Acceptance of any lesser standard means that we agree that National Service men and women must "make do" with less skilled specialists during their Army service than they have at their disposal in civil life. That proposition cannot seriously be defended. I therefore require the Army specialist surgeon to have at least five years' experience in his subject acceptable to the Council of the Royal Army Medical College, and in addition to have a Fellowship of one of the Royal Colleges of Surgeons, or an equivalent surgical degree. To these conditions there can be no exception.

There are, however, positions in the Army surgical service which can be filled by men of something less than full specialist status. The title of Graded Surgeon now given to these officers might be continued, but recognition as graded surgeons should be withheld until an officer has had at least three years' training as a surgeon of a nature acceptable to the Council of the Royal Army Medical College, and, preferably, has passed the Primary examination of one of the Royal Colleges of Surgeons.

When the method of attaining specialist and graded status in the Army is examined, one difficulty presents at once. All entry to the regular Army is by short service commission, and a young officer is not assured of his regular commission until nearing the end of his four years as a short service officer. It ought to be possible for a young officer to be assessed by the Consulting Surgeon in his Command early in his service, and if a decision could then be taken that here is an officer worth training, he should be assured of a first-rate training, and he could look forward to a career in surgery. He would then be able to plan ahead without the disruptive hiatus which sometimes alienates possible recruits, and his studies would merely be a continuance of the study of medicine which after all represents what was presumably the officer's main interest in life when he adopted the profession.

Having obtained our surgical recruit, the details of his training now demand examination. What the Army needs most is general surgeons, and with few exceptions at this stage of our development, training should be directed to producing general surgeons. If in the future it should prove possible to spare men for what may be called the ultra-specialisms in surgery, then a general training will prove to have been time well spent. In the training of young army surgeons we must use both military and civilian material.

there were many opportunities for medical work—maybe as junior M.O. in a battle-ship. Most men who were well reported on, and who were professionally keen, were then given an opportunity of being appointed to a hospital for general duties. It was usually during this period that one's thoughts of specializing began to develop and one gradually took up the more intensive study of one's particular choice. Many doctors are not anxious for nor indeed are all suited for the responsibilities of hospital work; these will more naturally tend towards work in barracks, sick quarters, ships, &c., rather than in hospitals. One might describe them as the general practitioners of the Navy.

(2) Broadly speaking there are two schools of thought on the selection and training of our specialists:

(a) That they should be part-time specialists—doctors with a broad knowledge of naval life and conditions who have taken up a particular subject for special study and practice. This is the present system and is comparable with the provincial town part-time specialist. Most of our specialists in the Royal Navy have higher degrees or diplomas in their speciality and are encouraged and given facilities to obtain such: others though not possessing higher degrees may often be considered by their fellows as outstanding in their particular speciality. This again conforms with civilian part-time specialism.

The general scheme of service in the Royal Navy before World War II was that once at least in each rank, say approximately during each six-year period, one served a commission in a sea-going ship, lasting about two to two and a half years. It is an old naval tradition that after being for any length of time on land and associating with land-lubbers one needs to refresh oneself with deep blue water (and possibly some duty-free gin); thus enabling the naval officers of *all* branches to keep in touch with the special requirements and changes in naval life. The ship was (and maybe it still is) the real unit of naval life. It represented a complete cross-section of the whole service and it is only at sea that one meets with and hears the problems of every other branch of the Royal Navy both officer and rating. It was considered of the greatest importance that every specialist should have the background of the life at sea in order that every man's particular work and duty should be considered if and when he came to be seen or treated in hospital practice.

(b) That the choosing and training of the Service specialist should conform with that of the whole-time specialist of the teaching or large provincial hospitals. He should be chosen when young, and the pursuit of knowledge in his speciality should never be interfered with. Every facility should be given for attendance at refresher post-graduate courses and for attaining higher degrees. Such specialists would staff the naval hospitals at home and overseas, and would, of course, move around at much less frequent intervals than at present, when reappointments occur every two or three years. This would ensure continuity in a particular hospital and obviously should enhance the skill of the specialist in his particular line.

If this scheme was adopted two different classes of doctors in the Royal Navy would arise.

(a) The general practitioners—so to say—who would be appointed to ships, barracks, shore training establishments, dockyards, &c., and possibly to general duties in hospitals.

(b) The whole-time hospital specialist—junior and senior grades.

The staff of naval hospitals (nursing sisters, sick berth ratings, and V.A.D.) is at present mobile just like the doctors.

One could not expect whole-time specialists to accept this; part of their whole-time organization must be founded on the choosing and keeping together of a team; hence the whole hospital organization would need revision.



is not expected to be fit to resume duty within three months shall be invalided home, where he can be near his friends, where improved facilities for treatment exist, and where he will not be an incubus to the Army on foreign soil. This state of affairs is familiar to all surgeons practising amongst Britons abroad, and is not peculiar to the Army.

Finally, when it is recalled that reservists and pensioners are cared for by civilian services or by the Ministry of Pensions, and do not form an Army liability as do veterans in America, it is evident that surgery in the Army may occupy a somewhat restricted field. While this is so, it is still true that great numbers of our young men and women are exposed annually to the hazards of trauma and disease during their Army service, and these young people must be provided with an adequate surgical service.

If the Army is to get the men of the calibre I envisage, the pay of a surgeon will have to be equal to that of his colleague in a civilian surgical service plus compensation for moves, family separations, &c. It must be possible to rise in rank while continuing to practise surgery. In this respect a great advance has been made since before the last war, but even now it is doubtful if the importance of surgery and surgeons to the Army is sufficiently appreciated. A competent and respected surgeon in an Army peacetime station abroad is of immense value; his successes are dramatic; his failures are disastrous; all are prominently in the public eye, and no one who has not worked in small Army communities can have any idea of the confidence which a skilful and well-liked surgeon gives to the community. The converse of course is equally true.

In war medical arrangements for active operations are governed predominantly by surgical considerations. In peace, surgical considerations always bulk largely in medical planning, and public opinion in the Army of to-day is always most anxious to have surgical aid on its doorstep if possible.

It should be quite unnecessary for an Army surgeon to forsake surgery for administration in order to rise to high rank. In fact I believe that a well-trained surgeon whose skills have been kept polished by constant practice, and whose mental processes had been kept sharpened by constant contact and discussion with his colleagues in civil life, is outstandingly fitted to take higher appointments in a service where surgical knowledge and experience are of such value. It is quality of mind rather than actual experience of the duties involved which are of importance and count most in selecting men for high appointment in most walks of life.

It may be possible for a surgeon to continue the active practice of his speciality combined with administrative duties as he attains higher rank. This symbiosis is not unknown now in the Army, and is well known to Deans of medical schools, to Medical Directors of certain large hospitals in civil life, and to many others.

I consider that the reward aspect is highly relevant to this Discussion. It is only by ensuring an adequate training with the promise of a satisfying career to the surgical aspirant at the outset when his enthusiasm is brightly lit, and eventually an adequate reward which will satisfy a critical mind that we can hope to attract men of the calibre we need. These must be men upon whom we can rely to furnish, for that part of our population which forms the Army, a surgical service comparable with that available to the rest of the population; and a service with which we as citizens can be content.

In the Army now we still do not get our potential surgeons early enough in their careers, and we sometimes find difficulty in ensuring continuity of experience. We have not yet got any formal system of exchange with civilian surgical services; and we are allowed only one period of one year during which an officer can formally be attached whole-time to a civilian surgical unit. In the Army we are at present squeezing from all sources every ounce of surgical experience within the limits imposed by regulations, but I am acutely conscious of these limitations. Post-war conditions

On the military side a surgical aspirant must be posted to a large military hospital as a trainee, and there his training must be the direct concern not only of the officer in charge of the surgical division, but of the consulting surgeon of the command. In the army the officers now holding divisional appointments are all well able to guide a trainee at this stage of his career. Besides acquiring surgical experience during this time, a young surgeon must be engaged in a study of basic medical sciences which will enable him in due course to present himself for a Primary Fellowship examination. The difficulties confronting a trainee in certain stations abroad (where most men will probably have to begin their training) are indeed formidable, but are surmountable if he is given the necessary help and encouragement. At this stage of his career it is most important also to secure continuity of training, and this must be ensured by some means more mandatory than merely by sympathetic administration.

At the same time all opportunities of enlarging experience in civilian hospitals must be seized by trainee surgeons wherever they may be serving. At home this presents no great difficulty as a rule, though facilities naturally vary in different stations. The Director of Surgery will always arrange suitable postings for his trainees to take advantage of any specially good openings which may exist in civilian surgical centres. It is regrettable but true that never since the last war have we been able to fill with a continuous stream of trainees all the proffered openings in civilian hospitals.

Abroad the situation is different now to what it was even before the last war. In India we have lost the missionary and other hospitals in which young Army surgeons were able to enlarge their experience and practise their skills. Facilities in civil hospitals do exist still in certain stations in the Far East, and in parts of the Middle East for trainees to widen their experience, but the scope here is lessened since before the war. So far, then, training has been carried out mainly in military hospitals, but also, to a lesser extent in civil hospitals.

At the Royal Army Medical College is offered what is called a Senior Officers' Course of some eighteen months' duration, of which the last twelve months are devoted solely to the study of an officer's speciality. Up to now surgical training should have been continuous, and in my view a surgeon, possibly graded by now, should not be allowed to join the College course until he has passed at least a Primary Fellowship examination. Indeed, the officer who benefits most by the year's intensive specialist training is one who already has passed his Fellowship.

This year of specialist training is best spent, and is in fact now spent in a large civilian surgical service. The time is all too short but I want for the surgical aspirant at this time wide clinical experience and the acquisition of operative dexterity, since now clinical material becomes available on a more generous scale than that to which he may hitherto have been accustomed.

At the end of his five years' experience in surgery, provided he has by then obtained a Fellowship or equivalent degree, a surgeon might apply to the Royal Army Medical College Council for recognition as a specialist. Some officers might for various reasons never be able to satisfy the Council of their right to specialist status, and in consequence might have to retain throughout their service the graded status they had earlier acquired.

While the Army is recruited mainly from the younger age-groups, it does include men and women of all ages up to 60, and the treatment of the families of officers and men in ever-increasing numbers forms quite an appreciable portion of the duties of the Royal Army Medical Corps, at any rate in stations abroad. It is fair to say, however, that those serving in the Army do start off as a rule fitter men and women than are found in civil life.

A further limitation on surgical practice in the Army is that imposed by foreign service. Policy in commands abroad requires that a soldier in danger of his life from malignant or certain other diseases, or a soldier who by reason of disease or injury

It is at this stage that further study, including attendance at civilian hospitals and clinics, is imperative in order to maintain the high standard of professional knowledge which must be an essential part of a Service specialist. It is therefore suggested that:

(a) Medical officers desiring to specialize be given every aid to study and qualify for their higher diplomas.

(b) That having attained the status of specialist they should continue to attend regularly at civilian hospitals, that such attendance be regarded as an integral part of their Service duties, and that they hold an official post in the civilian hospital which they attend, e.g. clinical assistant.

**Senior officers.**—Having the years of experience of a Service life behind them and the possession of a higher surgical qualification in addition should not preclude these officers from a pursuit of further knowledge and experience. The duty of such a senior officer is to teach his juniors, and this can only be done if senior officers are up to date both in experience and knowledge of their speciality and Service needs generally.

**Surgeon Captain W. D. W. Brooks:** As a preliminary to training, the proper selection of specialists in the Services is fundamental, and there would seem to be no reason why intelligence and aptitude tests should not contribute their part so that the right men are chosen for clinical advancement. It is important that this selection should take place at an early stage, and that when selected the potential specialist should spend at least a year in a teaching hospital, learning the essentials of his speciality. Thereafter, on appointment as a specialist, there is a continuous need for practice in that speciality. This implies that interruptions in his work by the necessity of going to sea should be reduced as far as possible, and that since the number and variety of cases likely to be available in some specialities may well be limited, continuous liaison with teaching hospitals is desirable. The latter should consist not merely in attendance and tuition, but also in having a regular position with clinical responsibility including teaching duties. It would seem also to be desirable to increase the proportion of cases available for specialist work in Service hospitals by opening them to the wives and families of all Service personnel.

Finally, in order to attract men of the highest quality as Service specialists it is essential that promotion to the senior ranks as clinicians should be a recognized possibility, to which end more senior clinical positions such as local as well as Service consultants might be created.

**Dr. H. L. Marriott:** The encouragement of specialism within the Services is desirable provided it is not allowed to run riot. The advantage of having regular Service specialists of high standing is that there will always be available men of professional knowledge to influence policy and to raise the standard. There is no doubt that many young men do not join because they think they will be debarred from a satisfying professional future.

The Service specialist must be first class. He must be quite equal to his civilian counterpart. It is a matter of selecting good men to begin with; then giving them a good initial specialist education and subsequently following it up with sustained training for the rest of their lives.

However, all the Services are having considerable difficulty in finding men of almost any quality for their intake as regulars. A few days ago the Director-General of the Army Medical Service informed me that the intake of officer recruits was almost nil. That is to say that not only was the intake quite inadequate in quantity but also the quality is down to a matter of accepting what recruits can be got.

This aspect has not so far been mentioned but it is a matter of the greatest importance. The lack of recruits is chiefly due to the relatively unattractive terms of service offered by the military services. It is, therefore, most important that those terms should be altered and we civilians should do our utmost to help the regulars in securing such

have undoubtedly improved the training which it has been possible to give Army surgeons, but in my view this is still far from satisfactory.

To achieve the complete training I am aiming at, it may be necessary to integrate the Army surgical service closely with one or more large civilian surgical services so that posts are readily interchangeable at regular intervals. Such an integration would be easy nowadays, and the benefits would be of inestimable value.

**Group Captain F. W. P. Dixon, M.B.E.:** This subject resolves itself into two main factors: (1) The needs of the Service for clinicians of experience and the requisite professional status; and (2) the prospects and incentives offered to medical men to take up a clinical career in the Service.

(1) It is essential that regular officers be recruited, in order that at least a nucleus of men skilled in their speciality will be available for the needs of the Service in peacetime. It is also of the highest importance that these specialists should have the clinical experience equal to that of their colleagues in civil life. At present, such officers with the exception of a very small number are serving on temporary commissions of eighteen months to two years, and it is obvious that such a condition of affairs is most unsatisfactory from all points of view.

(2) What has the Service to offer to a young man who aspires to specialization in clinical medicine or surgery; how does the prospect of a Service career compare with civil life?

#### GENERAL CONSIDERATIONS

(i) It is the general feeling that specialist work solely confined to Service duties is not enough to keep a man up to date with all aspects of his speciality, and therefore attendance at a civilian teaching hospital (if reasonably possible) for one or two days each week is desirable.

(ii) The prospects of promotion should be at least as good as those of his colleagues in the administrative branches of medicine, and ultimate promotion to the higher ranks should not jeopardize his future in clinical work. It is generally agreed that a man really begins to reach true specialist ability and knowledge after many years of experience and practice of his subject; it is therefore felt that specialists should be retained in their duties despite promotion to senior ranks.

(iii) Every opportunity should be given to officers in the way of study leave, attendance at civil hospitals, &c., to improve their professional knowledge, and to maintain a close liaison with their civilian colleagues.

**Junior officers.**—Once an officer has been granted a permanent commission and has expressed a desire to work and study in a special branch—and providing he is considered suitable—then every encouragement should be given him to achieve his aim. Such an individual is to become not only proficient in his medical or surgical speciality, but at the same time to take up an added speciality, i.e. the career of a Service medical officer in the Royal Air Force, the study and knowledge of which is gained only by personal experience and contact with all branches of the Service. It is therefore essential that a junior officer in his early years of Service life should be posted first to active flying units, and thereby acquire first-hand knowledge of the special problems, social and medical, and flying experience at first hand. Later he should be posted to a Service hospital, and commence his studies, for a higher degree or diploma.

On obtaining his Primary Fellowship and having completed a certain number of years in his special duties he may then be classed as a graded surgeon. A further course of studies and experience, together with the Final Fellowship diploma, then brings him into the specialist class. It is during these years of study that every consideration should be given by the Authorities for opportunities to attend lectures and courses for examinations. This is already provided for in the study leave with pay and allowances granted to officers in the Regular Service.

I met only 6 cases of gall-bladder disease in R.A.F. personnel, whereas in pre-war days in civilian practice I saw that number every month and, not infrequently, every week. Numerous examples could be cited and an impressive list of "absent" diseases drawn up. Now this limitation of material leads to the making of specialists who know "less and less about more and more" and on the surgical side, under peace conditions, into the gradual mummification of a surgeon into a herniotomist and minor orthopaedist.

The second difficulty is due to the posting of specialists. The geographical location and the "time factor" of postings are dictated by the needs of the Service; these are, of course, paramount and must of necessity take precedence over any other consideration; nevertheless, the periods of service overseas, in small units, in sparsely populated areas, are a real obstacle to the full development of specialist skill and the maintenance of a high pitch of professional efficiency.

There is, of course, the other side of the picture, namely the opportunities inherent to Service medicine. We are apt to overlook them and thus a little emphasis may not be out of place on these opportunities offered by the medical aspects of certain problems directly concerned with the Fighting Services. A few instances will suffice. In the Royal Air Force, unique opportunities present themselves to study the problems of the effect of noise on hearing, of deafness at altitudes, of night vision and of many problems of physiology, which form part of aviation medicine. In all three Services injuries due to frostbite, or immersion, offer a field of study in peripheral vascular disease. That the great advances in tropical medicine, hygiene and preventive medicine were due in great measure to the Service doctors is well known to all. Many unsolved problems in biophysics and chemistry face the medical profession now—the detection of radioactive substances, the symptomatology, prevention and treatment of injuries by fission products and by chemical and bacterial warfare—all these are in fact opportunities for the Service specialist of tomorrow, and should therefore be taken today.

What are therefore the special problems?

Firstly to attract the right type of men by providing facilities for professional advancement.

Secondly a plan for post-graduate specialist education. Such a plan must integrate the Service needs and the professional needs. It requires sympathetic consideration by those in authority, a careful selection of the would-be specialists and opportunities for training and the practice of the speciality.

Training is needed firstly in the basic sciences—anatomy, physiology, pathology and applied biophysics; these could be given within the Service to the junior officers, and if necessary such training should alternate with or be concomitant with the period of service as a unit medical officer. Later, training in the clinical specialities with the view of obtaining a higher degree or diploma is essential and unavoidable; it is a *sine qua non* in civilian life and should be so in the Services.

It must be recognized that the number of specialists in the Services is limited. The fact that they are few makes it all the more important that the few should be select. Their fewness also makes it impossible to provide all the education within the framework of Service hospitals.

Certain needs are obvious:

(1) Postings of specialists or trainee-specialists should alternate between civilian and Service hospitals. All civilian hospitals, teaching, non-teaching, and special hospitals, should provide facilities for supernumerary posts—of all grades, residents, clinical assistants, registrars, chief assistants, assistant physicians or surgeons. There is an untapped source of clinical wealth at the disposal of the Service specialists; there is also the desire of most civilian hospitals to accept Service doctors to such posts for periods of three or six months or longer.

an improvement that an inflow of high quality recruits into the Services will begin. Unless this happens the efficiency of the Services is bound to deteriorate and there can be no question of a first-class specialist service.

**Good initial training:** The same essentials apply to the training of the Service specialist as apply to the training of a civilian specialist. That is, apprenticeship, as a registrar, for a period of not less than three years under good teachers in a good hospital with active charge of cases and with teaching responsibility. These are the essentials.

**Good continued training:** If the Service specialist is to maintain a high standard, he must be kept up to it in the same way as the civilian specialist is kept up to scratch. He must work fairly frequently in good hospitals in which he has active charge of cases and he must teach.

Can Service hospitals provide facilities for adequate initial and continued training? The answer, I think, is that they cannot except to a limited degree. Service hospitals are not large enough to train an adequate number of specialists nor do they have a sufficiently wide range of clinical material. Therefore, the solution of the initial and continued training of Service specialists must be a matter of a liaison arrangement with civilian teaching hospitals. I would underline *teaching hospitals*.

I cannot see why a satisfactory arrangement cannot be arrived at whereby Service specialists are *secured* special posts in teaching hospitals which they should occupy as a matter of right and not as courtesy and in which they should be given a measure of active charge of patients and definitely, and most important, made responsible for teaching. At the present time most teaching hospitals have a large number of additional registrars demobilized from the Services. The arrangement has worked well and the men have received good training. Why cannot there be a permanent arrangement for the training of a much smaller number of Service specialists? Once the Service specialist has passed the apprentice stage he still needs to come back frequently and work in the atmosphere of teaching hospitals. This is especially true after periods abroad. Surely, it should be possible to incorporate one or two such specialists into the organization of each teaching hospital.

There has never been such a favourable opportunity as now exists for the inauguration of such a scheme. It is a matter of the three Services getting together and pushing for it hard, and I am sure that the desired organization can be brought into being. If a drive is not made now the favourable opportunity will pass.

**Sir Stanford Cade, K.B.E., C.B.:** A discussion on the post-graduate education of specialists in the Services should deal with the difficulties, opportunities and problems inherent to the practice of specialists in the Services. The aim of specialization is of course the same in Civilian as in Service practice, namely the acquisition of special skill and experience, therefore the standard must also be the same and complete equality of professional attainments with colleagues in civilian life possible of achievement.

What are the special difficulties inherent to the Services? These are mainly two: Firstly the limited type of clinical material. This was forcibly brought home to those of us returning to civilian hospitals after a few years in Service practice. Most of us felt it so greatly that a period of rehabilitation or acclimatization was necessary before we became once again completely at ease in our routine work. The clinical material in Service hospitals consists of young adult males—probably to the extent of 90%. The majority of patients in civilian hospitals are not young adult males, half the patients are female, about one-third are between 50 and 70 years of age; children are the source of valuable experience, although pædiatrics is a speciality in itself. This narrower field is still further narrowed by the type of illness most common in the young age-groups. A few instances would suffice: during my six years of War Service,

## Section of Dermatology

President—J. E. M. WIGLEY, F.R.C.P.

[May 19, 1949]

**Periarteritis Nodosa.**—H. W. BARBER, F.R.C.P.

L. C., male, aged 30. This patient first consulted me on January 6, 1948, for a condition of the right side of the lower back, which had been noticed during the previous winter. There was a scar with apparently rolled edges and slight ulceration at one point. Above and below there was a bluish discoloration suggestive of an angiomatous naevus, but it was clearly similar to that observed later on the arms (livedo-like form of periarteritis nodosa). I thought that this lesion on the back was probably a superficial basal-celled epithelioma and it was excised, but the histological report was as follows :

"The skin shows a superficial non-specific chronic ulcer, accompanied by peri-follicular infiltrations of lymphocytes, histiocytes and eosinophil polymorph leucocytes. There is no evidence of malignant disease of the epidermis nor of tuberculosis. The picture is consistent with a non-specific granuloma with a predominantly eosinophilic reaction." July 26, 1948.

I did not see the patient again until early this year shortly after he had consulted Professor Miescher in Zürich. At that time both arms were involved above and around the elbow-joints. There was the same livedo-like, violet discoloration that was present on the back with necrotic ulcerations which were extremely painful. There was also some diffuse oedema of the affected parts. The earliest sign of involvement of new areas was the violet discoloration. Then at one or more points a small scab would form, and beneath this the skin became necrosed, leaving an ulcer that gradually extended, but might heal spontaneously.

Professor Miescher tells me that he considered the affection to be primarily vascular, suggestive of a periarteritis and periphlebitis nodosa, or possibly a phlebitis migrans, or another form of endo- and perivasculitis ( ? lues). He also considered a primary necrosing pyoderma with secondary ulceration of the vessels, but did not think this likely in view of the evolution of the eruption. Wassermann and Kahn reactions were negative, and the blood-count was normal except for an eosinophilia of 7% and slight monocytosis and lymphocytosis.

My own view was that the condition was probably a periarteritis nodosa of the skin, and I elicited the history that previous to the onset the patient had had several intensive courses of sulphonamides.

He was admitted to Nuffield House on March 6, 1949, and seen in consultation with Dr. Ralph Kauntze. The investigations were of course designed to discover any evidence of visceral involvement.

**Blood-count.**—Slight tendency to macrocytosis of the red cells ; lymphocytosis (46%), no eosinophilia, slow B.S.R.

Urine : No abnormality, cultures sterile.

Blood cholesterol : 120 mg. %.

Blood urea : 23 mg. %.

Plasma proteins normal.

Biopsy from edge of ulcer on the left arm : " Serial sections reveal a number of small arteries of 1 mm. diameter (approx.) with marked perivascular fibrosis and chronic inflammatory cells with disorganization of the media, which is strongly suggestive of periarteritis nodosa of chronic type."—S. J. De Navasquez.

Dr. Geoffrey Evans: When I saw this man a diagnosis of periarteritis nodosa had been made. With periarteritis nodosa of this severity and with no treatment available to control the disease the outlook is very grim. Further examination of the case showed a granulomatous ulcerated area like a broken-down gumma. At my suggestion Dr. Benjafield made an investigation (see his report). The possibility of this being a blastomycotic lesion of the skin arises and opens up other possibilities of treatment. The patient has been given potassium iodide since I first saw him, beginning with 15 grains daily. There may already be an improvement because what he has come to regard as typical of an early lesion, namely a purplish discoloured area on the right upper

(2) Acceptance of civilian patients—men, women and children—to Service hospitals to the full bed-state capacity. Such an arrangement would ease the burden of civilian hospital bed shortage and shortage of nurses. It would remedy the lack of variety of clinical material and would establish a close liaison between Service and Civilian hospitals and their staffs.

(3) Pooling of the resources within the Services. In their main hospitals, large series of major cases could be collected—orthopædic, urological, plastic, tumour cases, tropical disease, &c.

(4) The Service personnel should for purposes of post-graduate clinical study be integrated.

(5) To plan, guide, direct, and supervise post-graduate study, a Director of Studies should be a full time post.

(6) Research is an integral part of post-graduate study. Research is individualistic—it should be encouraged and rewarded.

Other speakers were :

Lieutenant-Colonel A. Meneces.

Brigadier E. R. Boland.

Brigadier Ian Aird.

Surgeon Commander J. S. L. Coulter.

Group Captain C. A. Rumball.

Brigadier F. A. R. Stammers.

Brigadier H. C. Edwards.

Brigadier J. Bennet.

Brigadier D. Fettes.

Dr. J. G. Scadding.

Surgeon Vice-Admiral J. A. Maxwell.

Lieutenant-General N. Cantlie.

Air Vice-Marshal P. C. Livingston.

Wing Commander G. H. Morley.

Mr. C. Hope Carlton.



and plasma cells, some of the blood-vessel walls are thickened and have distorted lumina (fig. 2). The calf muscle is unaffected. The electrical responses of the muscles, and the electrocardiogram are normal. The Wassermann and Kahn reactions are negative.

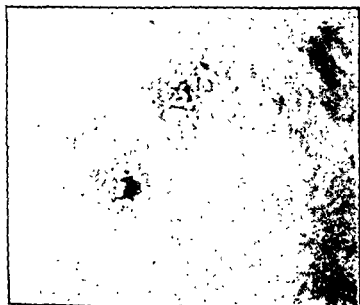


FIG. 1.—Shoulder region showing scarring. (Chronic stage.)

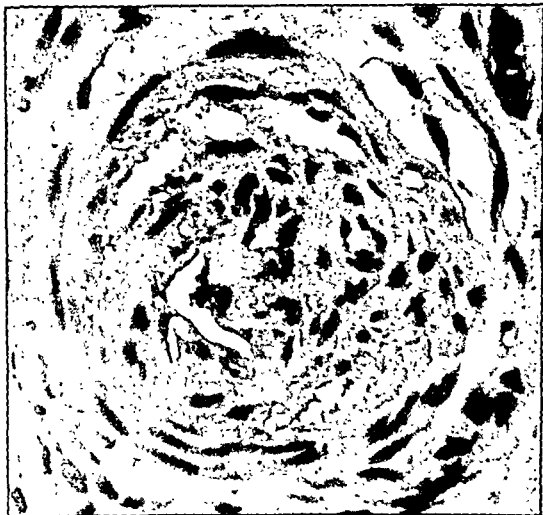


FIG. 2.—Thrombosed vessel in the deep part of the corium—recanalization. (Chronic stage.) ( $\times 500$ .)

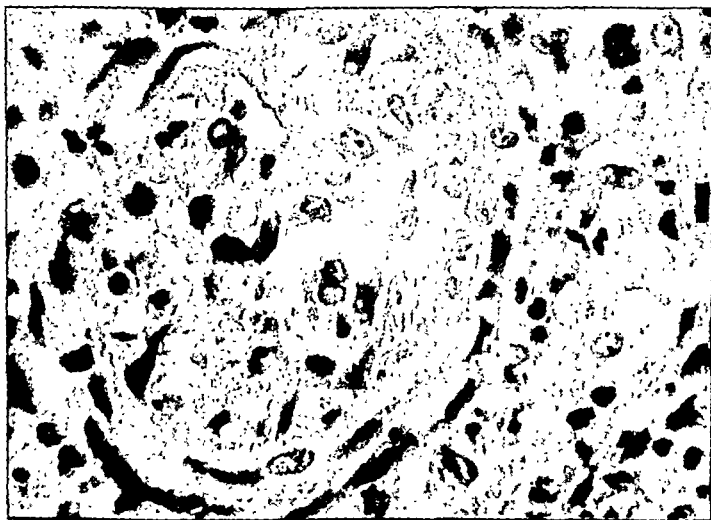


FIG. 3.—Acute inflammation involving vessel wall. (Acute stage.) ( $\times 600$ .)

Some features do not support the diagnosis of dermatomyositis, namely, the absence of muscular wasting and weakness, the normal muscle biopsy, the distribution of the lesions, and finally the recent appearance of tender nodules.

The alternative diagnosis was polyarteritis nodosa.

POSTSCRIPT.—Microscopical examination of one of the tender nodules showed an arteritis with acute inflammatory exudate (fig. 3). Dr. A. M. Barrett, the pathologist, considered the picture compatible with polyarteritis nodosa, though involving unusually small vessels.

A ground-up nodule was sterile on culture (Dr. Gleeson-White).

Dr. H. W. Barber: My opinion is that this case, like my own, is one of widespread periarteritis

arm, has not progressed and has indeed got rather smaller. Since beginning the potassium iodide, however, the largest ulcer has become larger and the black areas of necrosis have also increased.

Dr. Benjafield and I thought that perhaps the sections showed the spores deep in the tissues: that the early lesions which precede ulceration may lie deep in the dermis, and that it is these lesions which look like periarteritis nodosa. The points against the diagnosis of periarteritis nodosa are that it is a local lesion of the skin and there is no constitutional or systemic disease; in the second place there are no skin nodules to be felt. It is for these two reasons particularly that the alternative diagnosis of blastomycosis suggested itself to me.

Dr. J. D. Benjafield: I removed a small scab at the edge of a lesion near the right elbow. After softening in 10% liq. potassii hydroxidi this showed numerous double-contoured rings and various other pieces of fungus. I also prepared cultures from the pus from the floor of a lesion on plates of maltose-agar. These yielded a pure and copious growth of fungus at room temperature, which macroscopically resembled *Candida albicans*. Subsequently this culture was handed to Professor Duncan, who had suggested that it resembled *Candida albicans* but later, on subculture, stated that the fungus exhibits the characters of *Endomyces* (non-pathogenic). The other point that may be of interest is that I handed over a culture of the fungus to the bacteriological department of St. George's Hospital for animal inoculation.

POSTSCRIPT.—An emulsion of the organism was given to two guinea-pigs intravenously. No apparent effect was produced.

Dr. Ernst Sklarz: I examined fresh preparations under the microscope and later on the cultures and was convinced that the fungi were blastomycetes. They were as typical as any I saw in Professor Buschke's laboratory at the Rudolf Virchow Krankenhaus in Berlin, where we received material from all over the world, as it was Buschke who in 1894 first described skin blastomycosis in man. Skin blastomycosis in veterinary medicine was not unknown, and human cases are not as rare as is sometimes supposed.

The case demonstrated to-day could also be diagnosed clinically as a fungus infection; the black sloughs are a little uncommon but could be explained by superinfection.

Dr. H. R. Vickers: We have had about six of these cases in Sheffield during the last two years. They have been collected by Dr. Sneddon and I do not know the exact details of them all. The case now shown is characteristic of some of those we have been seeing. The disease starts with small raised hæmorrhagic nodules occurring anywhere on the skin. Sometimes these nodules disappear; in other cases they go on to produce ulcers, either on the skin alone or affecting the deeper tissues. I think that the majority of the cases had received sulphonamide and all but two have died. One patient at present appears to be controlled by anti-histamine drugs but the outlook in these cases is very depressing. I have no doubt at all that this is a case of periarteritis nodosa.

Dr. Sydney Thomson: I fail to see why we should be told that this is a typical case of blastomycosis. The picture here presented is quite remote from that appreciated by those of us who have seen some of those cases. There are no signs whatever of the typical papillomatous changes, no obvious granulomatous infiltration and no traces of the intra-epithelial abscesses which form so typical a part of the histological picture. So far as the organism is concerned, we should remember that a common and very misleading secondary fungus is the chlamydospore, particularly in chronic ulcerations. This case would seem to be identical with the cases of periarteritis nodosa seen in Sheffield and elsewhere.

For Diagnosis ? Dermatomyositis.—A. LYELL, M.B., and C. H. WHITTLE, M.D.

M. L., aged 22.

This previously healthy man's illness started seven years ago with "rheumatic fever". The pains were universal and lasted two months.

Two years later he had a more severe attack, with generalized and agonizing muscle pains, and paralysis. During the attack his face swelled, and for a week he could not see for the oedema of his eyelids. He sweated profusely during the illness, which kept him in bed for a year. His weight at the start was 12 st., and at the end 7 st. 5 lb.

Recovery was slow and was complicated by the gradual appearance of skin changes, which involved particularly the region of the shoulders and the calves.

He now presents the following changes in the skin: The texture is altered owing to a thickening and toughening of the corium; because of this the biopsy of the calf was extremely difficult, the injection of local anæsthetic slow and painful; the corium cut with difficulty, and the wound gaped and was hard to close. Failure of the inelastic skin to conform to the movements of the arm is perhaps responsible for the ulceration round the shoulders (fig. 1). A mauve mottling of this region, and also of the forearms and calves, shows up better in the cold; the calves in addition are brown. Some of these lesions are tender. In the last few days tender nodules have appeared over the forehead and forearms.

The clinical diagnosis was dermatomyositis.

There is a creatinuria of 0.57 gramme per litre (creatinine 1.25 grammes per litre). The sedimentation rate (Westergren) was 35 mm. in the first hour (March) and 37 mm. (May). A full blood-count is within normal limits, except for an eosinophilia of 9% of 8,000 white cells. Histologically the epidermis is normal except for increased pigmentation in the basal layer. The corium is thickened and there is a slight perivascular infiltrate of lymphocytes

there is proliferation of spindle cells, round cells and a few eosinophils. One or two mitotic figures are also present. Blood pigment, both extracellular and intracellular, is abundant.

The histology shows features of Kaposi's disease.

**Lichen Planus.**—G. B. MITCHELL-HEGGS, O.B.E., F.R.C.P., and P. FORBES BORRIE, M.R.C.P. Mrs. B. D., aged 58.

*History.*—Three and a half years ago she noticed a patchy loss of hair on the scalp with severe irritation and much scaling. A few weeks later, there was a rash round her waist with slight soreness which cleared completely in two months with ung. acid salicyl. 2%.

The irritation and scaling of the scalp cleared up with lotio hydrarg. perchlor. and acid salicyl., but she continued to lose her hair slowly and without any regrowth up to and including the present time, in spite of further treatment with thorium X and U.V.L. Three months ago, there was a recurrence of the rash on the chest and arms.

*Past history.*—Menopause at the age of 47. Otherwise nil.

*Family history.*—Married, no children.

*On examination.*—There is a cicatricial alopecia involving nearly the whole of the scalp but leaving a margin of dry grey hairs round the circumference, where there are numerous erythematous follicular papules. Similar papules together with the loss of hair are also found in the axillæ and in the pubic region.

On the upper part of the back, shoulders, breasts and sub-mammary region, there are grouped skin- to pink-coloured follicular papules with keratotic tops from which protrude small spines. Around the waist and also in the biopsy scar below the right breast, there are typical lichen planus papules.

Mucous membranes clear.

All other systems N.A.D.

*Investigations.*—Biopsy report: hyperkeratosis and follicular plugging. Acanthosis and irregularity of the papillæ. Some increase of fibrosis in the corium. No evidence of any actual inflammatory change.

W.R. negative.

The following cases were also shown :

**Riehl's Melanosis.**—Dr. BETHEL SOLOMONS, Jr. (for Dr. H. CORSI).

**Necrobiosis Lipoidica Diabeticorum.**—Dr. A. LYELL and Dr. C. H. WHITTLE.

**Case for Diagnosis. Purpura.**—Dr. R. E. CHURCH and Dr. C. H. WHITTLE.

**Case for Diagnosis. ? Angioendothelioma.**—Dr. F. RAY BETTLEY.

**Fixed Drug Eruption.**—Dr. G. B. MITCHELL-HEGGS and Dr. P. FORBES BORRIE.

**Sarcoidosis.**—Dr. F. J. JENNER.

**Tar Dermatitis.**—Dr. F. J. JENNER and Dr. HENRY HABER.

**Sebocystomatosis.**—Dr. D. S. ANDERSON.

**Multiple "Glomus-Tumours".**—Dr. D. S. WILKINSON.

(These cases may be published later in the *British Journal of Dermatology*.)

[June 16, 1949]

**Lichen Sclerosus et Atrophicus.**—R. T. BRAIN, M.D., and H. HABER, M.D.

S. D., a girl, aged 10, developed the first lesion nine months ago on the site of a bruise in the middle of the back. The mother stated that the bruise turned blue and mauve and a brown crust formed a few weeks later. Other lesions appeared, the first on the right shoulder, another on the right hip and a third between the buttocks. There were no symptoms and patient's general health was good. There is no family history of skin diseases.

*On examination.*—The primary and largest lesion was a sharply defined plaque 3 by 4 cm. in the lower dorsal region, mid-line. The surface was covered with a dusky brown, heaped-up collection of horny scales presenting a peculiar creasing of the surface, with a starlike pattern in the upper part; in the lower part the scaling followed the natural lines of the skin. Towards the edges of the discoloured central scale the colour was paler and merged into an atrophic border, 2 mm. wide, of paper-white colour. Just above the large lesion was a smaller patch about 1 cm. in diameter, and on the shoulder a 3 cm. plaque markedly elevated, of a violaceous colour, and covered by adherent scales, which showed silver psoriasisiform cracks on scratching but no capillary bleeding. A 2 cm. plaque on the right hip showed similar cracks but was somewhat more raised centrally. At the top of the gluteal

nodosa affecting the skin. I understand that the patient had previously been given sulphonamide for his acute illness (? acute rheumatism).

**Dr. F. Parkes Weber:** The diagnosis of dermatomyositis does not exclude by a long way the diagnosis of periarteritis nodosa. They are very much allied and it is quite possible that periarteritis nodosa might be a feature at a stage of a case of dermatomyositis.

**Dr. H. Haber:** The vascular pattern seen in that case reminds one of Ehrmann's livedo racemosa, a condition first found in tertiary syphilis. But other conditions affecting the cutaneous vascular network may produce the same clinical picture. (Tb. endocarditis, exposure to cold.)

Histologically there is usually an obliterative endarteritis to be found situated between cutis and subcutis.

**Dr. R. T. Brain:** Dr. Haber has not mentioned that he himself has done some original work on this condition. From what I have seen of the histology of periarteritis nodosa, I think that other inflammatory conditions can produce vascular lesions which may be attributed to this rare and obscure disease.

**Balanitis Xerotica Obliterans.**—P. D. SAMMAN, M.R.C.P. (for J. E. M. WIGLEY, F.R.C.P.).

H. P., aged 60.

*History.*—Throughout his early life this man had a tight prepuce which would retract only with difficulty and at times with tearing. He was married in 1917.

In 1935 he developed a wart on the prepuce which was treated by circumcision. The glans penis at that time was normal.

In 1937 he noticed some scaling around the urethral orifice which cleared in a matter of weeks.

1938: There was some scaling of the glans with formation of hard skin. As the scale disappeared the skin below was normal.

1942: A small raw area developed when a scale separated and this healed with the use of powder.

1944: Other raw areas appeared and healed more slowly.

December 1948: Another raw area formed and has persisted up to the present time.

Throughout he has had no pain and no loss of sensation. There has been no reduction of the urinary stream.

*On examination.*—The shaft of the penis is normal and there is little abnormality of the corona. Over the remainder of the glans the skin is shiny and atrophic; in places there is some thickening and evidence of previous ulceration. On the under surface near the urethral orifice there is an ulcerated area with sharply defined margin. Normally the ulcerated area is dry but at times there is exudation. The urethral orifice is only slightly stenosed.

**The President:** I showed a similar case to this about two years ago. It has been treated sporadically with testosterone.

**Dr. J. Sommerville:** I think I have seen two cases in all. In my experience they have not gone as far as this in regard to shrinking. I think it is open to doubt whether this is a case of balanitis xerotica obliterans.

**Kaposi's Hæmorrhagic Sarcoma.**—P. D. SAMMAN, M.R.C.P. (for J. E. M. WIGLEY, F.R.C.P.).

Mrs. L. P., aged 61.

*History.*—About seven years ago the patient noticed a patch of pigmentation on the front of the left ankle. This almost disappeared with adhesive strapping but during the next five years several more patches appeared which were more persistent and tended to become confluent.

Two years ago patches of a different colour appeared and have gradually increased in number, becoming confluent in places. They are slightly raised.

One year ago the ankle began to swell during the daytime, subsiding after a night's rest. This œdema has been slowly progressive. The right leg has not been involved.

*On examination.*—There are a number of plaques of a reddish-blue colour on the left ankle and one on the second left toe. Several are discrete, roughly circular and 1 cm. in diameter with clearly defined margins; they are slightly raised and infiltrated, others have become confluent giving a large irregular plaque. In addition to these plaques there is a patchy pigmentation of the ankle and considerable œdema.

Treatment has been small fractional doses of X-rays.

*Histology* (Dr. Henry Haber).—The epidermis is normal. The upper part of the corium exhibits a granuloma consisting of newly-formed small vessels, some of which show proliferation of their endothelial linings leading to obliteration of the lumina. Furthermore,

there is proliferation of spindle cells, round cells and a few eosinophils. One or two mitotic figures are also present. Blood pigment, both extracellular and intracellular, is abundant.

The histology shows features of Kaposi's disease.

**Lichen Planus.**—G. B. MITCHELL-HEGGS, O.B.E., F.R.C.P., and P. FORBES BORRIE, M.R.C.P. Mrs. B. D., aged 58.

*History.*—Three and a half years ago she noticed a patchy loss of hair on the scalp with severe irritation and much scaling. A few weeks later, there was a rash round her waist with slight soreness which cleared completely in two months with ung. acid salicyl. 2%.

The irritation and scaling of the scalp cleared up with lotio hydrarg. perchlor. and acid salicyl., but she continued to lose her hair slowly and without any regrowth up to and including the present time, in spite of further treatment with thorium X and U.V.L. Three months ago, there was a recurrence of the rash on the chest and arms.

*Past history.*—Menopause at the age of 47. Otherwise nil.

*Family history.*—Married, no children.

*On examination.*—There is a cicatricial alopecia involving nearly the whole of the scalp but leaving a margin of dry grey hairs round the circumference, where there are numerous erythematous follicular papules. Similar papules together with the loss of hair are also found in the axillae and in the pubic region.

On the upper part of the back, shoulders, breasts and sub-mammary region, there are grouped skin- to pink-coloured follicular papules with keratotic tops from which protrude small spines. Around the waist and also in the biopsy scar below the right breast, there are typical lichen planus papules.

Mucous membranes clear.

All other systems N.A.D.

*Investigations.*—Biopsy report: hyperkeratosis and follicular plugging. Acanthosis and irregularity of the papillae. Some increase of fibrosis in the corium. No evidence of any actual inflammatory change.

W.R. negative.

The following cases were also shown :

**Riehl's Melanosis.**—Dr. BETHEL SOLOMONS, Jr. (for Dr. H. CORSI).

**Necrobiosis Lipoidica Diabeticorum.**—Dr. A. LYELL and Dr. C. H. WHITTLE.

**Case for Diagnosis. Purpura.**—Dr. R. E. CHURCH and Dr. C. H. WHITTLE.

**Case for Diagnosis. ? Angioendothelioma.**—Dr. F. RAY BETTLEY.

**Fixed Drug Eruption.**—Dr. G. B. MITCHELL-HEGGS and Dr. P. FORBES BORRIE.

**Sarcoidosis.**—Dr. F. J. JENNER.

**Tar Dermatitis.**—Dr. F. J. JENNER and Dr. HENRY HABER.

**Sebocystomatosis.**—Dr. D. S. ANDERSON.

**Multiple "Glomus-Tumours".**—Dr. D. S. WILKINSON.

(These cases may be published later in the *British Journal of Dermatology*.)

[June 16, 1949]

**Lichen Sclerosus et Atrophicus.**—R. T. BRAIN, M.D., and H. HABER, M.D.

S. D., a girl, aged 10, developed the first lesion nine months ago on the site of a bruise in the middle of the back. The mother stated that the bruise turned blue and mauve and a brown crust formed a few weeks later. Other lesions appeared, the first on the right shoulder, another on the right hip and a third between the buttocks. There were no symptoms and patient's general health was good. There is no family history of skin diseases.

*On examination.*—The primary and largest lesion was a sharply defined plaque 3 by 4 cm. in the lower dorsal region, mid-line. The surface was covered with a dusky brown, heaped-up collection of horny scales presenting a peculiar creasing of the surface, with a starlike pattern in the upper part; in the lower part the scaling followed the natural lines of the skin. Towards the edges of the discoloured central scale the colour was paler and merged into an atrophic border, 2 mm. wide, of paper-white colour. Just above the large lesion was a smaller patch about 1 cm. in diameter, and on the shoulder a 3 cm. plaque markedly elevated, of a violaceous colour, and covered by adherent scales, which showed silver psoriasisiform cracks on scratching but no capillary bleeding. A 2 cm. plaque on the right hip showed similar cracks but was somewhat more raised centrally. At the top of the gluteal

cleft two hyperkeratotic lesions were present, and below these two other lesions showing a pearly white atrophy with some plugging and dimpling of the surface.

The Wassermann and Kahn tests were negative.

**Histological report (Dr. H. Haber).—**Biopsy taken from the hyperkeratotic patch of the back: The epidermis shows absolute and relative hyperkeratosis, follicular plugging and atrophy of the rete malpighii. The upper third of the corium exhibits extreme œdema leading to the formation of a subepidermal bulla. The adjacent parts of the highly œdematous area look homogeneous while the bundles of the mid-cutis appear to be slightly thickened. The arrectores pilorum show hydrops of their muscle elements. There is also perivascular and periacinous round-cell infiltration. The vessels do not show any changes, while the elastica appears to be pressed down by the œdema in the upper corium and normal in the rest of the cutis.

**Dr. Brain:** A child was brought to Great Ormond Street—one of Dr. Dowling's patients—who showed what I took to be simple morphœa on the shoulder, but about the body were very hyperkeratotic patches, with a thick, pearly type of scale, such as we now associate with lichen sclerosus. The sections showed œdema just below the epidermis, dilated coarsely plugged follicles, some atrophy of the epidermis and little change in the deeper vessels. It was the memory of this hyperkeratotic type of lesion which made me regard the present case as lichen sclerosus.

**Dr. E. J. Moynahan:** Is it suggested that the condition in this patient is really a superficial œdema, or is it due to destruction of the superficial papillary elastic plexus? The perineum is a fairly common site for lichen sclerosus et atrophicus, where there is probably the largest collection of superficial elastic fibres in the body and one wonders whether there is any connexion. Could the reticulum fibres in these regions be studied to see what happens to that network—particularly those fibres in the upper part of the corium where they join with the epidermis?

**Dr. Henry Haber:** The changes are confined to the upper third of the corium. It consists of homogenization and extreme œdema of the collagen in the stratum papillare and subpapillare. The elastica is only pushed down by the œdema and appears normal in the rest of the corium. There is no increase of reticulum fibres demonstrable in lichen sclerosus et atrophicus.

**Poikiloderma Atrophicans Vascularis (Jacobi-Lane Type).—**BRIAN RUSSELL, M.D.

Mrs. N. C., aged 49. Part-time shop assistant.

**History.**—Low-grade psoriasis since her 12th year, only involving extensor surfaces, treated for a few months with ointments.

Early 1947: Mottling, dryness, and discoloration of the skin appeared, first on the thighs, then on the trunk, neck and arms. There has been no itching. She had had no widespread treatment with tar, light, X-rays, or arsenic.

**Habits.**—Has taken tablets for rheumatism during the last six months. Had sedative tablets during the war years. Takes medicine for dyspepsia.

**On examination.**—Well-nourished woman. Over the neck, body, arms, forearms, thighs, calves, and feet is a mottled rash consisting of small brown macules, white areas, and red areas without obvious vessels. There is slight atrophic wrinkling. Over the upper chest are lichenoid, erythematous, slightly scaly papules. Inner side of both heels shows hyperkeratosis. There is no enlargement of liver, spleen, or lymphatic glands. Mucous membranes normal.

**Histology (Dr. Henry Haber).**—The epidermis shows an undulating surface with alternating atrophy and acanthosis of the stratum spinulosum. There is also liquefaction with round-cell infiltration of the stratum basale demonstrable.

The appearance of the epidermis is due to an infiltrate which in some places is subepidermal leading to atrophy. In other places the infiltration is situated deeper and here the epidermis shows acanthosis. The subepidermal infiltration consisting of round cells together with liquefaction of the basal layer leading to cleft between epidermis and cutis closely simulates the histology of lichen planus.

The elastica appears to be destroyed within the infiltrate.

**Investigations.**—Urinary creatine 0.02 gramme; creatinine 0.97 gramme in 850 c.c. twenty-four-hour sample.

X-ray of lungs, forearms and hands normal.

Wassermann and Kahn reactions negative.

Serum calcium 9.7 mg. per 100 c.c. of serum.

**Comment.**—This case conforms with the dermatosis described by Lane (1921), and the histology with that illustrated by Dowling and Freudenthal (1938), being inflammatory in character as opposed to the degenerative changes noted in dermatomyositis. They pointed out that Jacobi's original case might possibly be in fact a burned-out case of dermatomyositis. Downing and Edelstein (1947) reported autopsy on a man aged 67 who had suffered from poikiloderma atrophicans. The skin disease was regarded as having been

the primary cause of death. They point out the relationship in some cases to Hodgkin's disease, lymphosarcoma, or mycosis fungoides, and suggest the possible importance of damage to the skin from physical agents such as extremes of temperature or sunlight in the aetiology of the condition. Poikiloderma-like changes in the skin have also been reported following arspenamine dermatitis (Cannon *et al.*, 1942).

#### REFERENCES

- CANNON, A. B., KARELITZ-KARRY, M. B., and FISCHER, J. K. (1942) *J. Amer. med. Ass.*, 118, 122-129.  
 DOWLING, G. B., and FREUDENTHAL, W. (1938) *Brit. J. Derm.*, 50, 519.  
 DOWNING, J. G., and EDELSTEIN, J. M. (1947) *Arch. Derm. Syph., Chicago*, 56, 740.  
 LANE, J. E. (1921) *Arch. Derm. Syph., Chicago*, 4, 536.

#### Acrodermatitis Chronica Atrophicans (Herxheimer).—STEPHEN GOLD, M.B.

Mrs. M. J., aged 55, first came under dermatological observation at the age of 12 for psoriasis affecting the limbs, body and scalp. She was then treated in Berlin, where she lived, by Professor Pinkus. She still gets occasional patches of psoriasis. Sixteen years ago she first noticed a crinkling of the skin over the dorsum of the right hand. The colour of the involved area remained normal, but would turn blue on immersion in water. Six years later a small nodule appeared on the right elbow, and a year after two smaller ones on the left elbow. Five years ago the back of the right hand became a dusky red, and this abnormal colouring spread up the right forearm. During the past twelve months similar colour changes have appeared on both legs. Her general health has been excellent, though recently she has been troubled with rheumatism affecting ankles, elbows and shoulders.

*Family history.*—Psoriasis on maternal side, and probably on paternal side as well.

Biochemical investigations, undertaken at King's College Hospital in September 1946, gave no abnormal findings. She was diagnosed as a typical case of Herxheimer's acrodermatitis, and accordingly has been treated with systemic penicillin in conjunction with local X-irradiation, as advised by Professor Miescher. To date she has received 2 million units of penicillin and four applications of 100 r to the back of the right hand. As is shown by the moulage made before treatment was started, there has been a marked improvement both in colour and in texture of the involved skin. I now understand that Miescher recommends a much larger dosage of penicillin in the order of some 9 million units, and I am starting her on another course.

Psoriasis in conjunction with this disease has been reported by Pautrier, but, as in the present case, the combination is probably fortuitous. Laymon has also noticed an association of this condition with a rheumatoid type of arthritis. Recently Haxthausen has performed some grafting experiments in patients suffering from this disease. Normal skin, transplanted to an involved area, later takes on typical characteristics of this condition. Skin from an involved area, grafted to an uninvolved site, returns to normality. This suggests that acrodermatitis chronica atrophicans is not primarily a disease of the cutaneous surface, but more in the nature of a trophic, vascular disorder.

Dr. Brian Russell: In December 1947 I showed a similar case, a woman who also came from Germany, but who had lived in Spanish Guinea for the last ten years. This condition is reported to be much more common on the Continent than in England and Breuckmann, H. (*Arch. Derm. Syph., Berlin*, 1939, 179, 695) reported 9 cases, 7 of whom showed evidence of arsenical intoxication derived either from insecticides or wine contaminated with arsenic. My patient while in Spanish Guinea had eaten much fruit, which had previously been sprayed with copper sulphate, which, according to the supplying firm, contained one-third to one-tenth of a grain of arsenic per pound.

#### Chronic Moniliasis.—BERNARD A. THOMAS, M.D.

J. R., boy, aged 7.

*History.*—Apart from an early tendency to regurgitate milk (doubtfully attributable to the present complaint) the first sign was a speech defect, noted as soon as he commenced to talk and persisting to the present time.

At the age of 4 years, papules appeared on the cheeks and have recurred intermittently. At the same time, the inside of the mouth was found to be covered with white "thrush" and he began to have regular colds and coughs accompanied by considerable pyrexia.

At the age of 5 years, redness and scaling began on three fingers and subsequently dystrophy of the nails. In August 1948 pus began to exude from under these nails and, after two months, they became detached. A prominent crusted lesion on the nose also appeared in August 1948.

*On examination.*—The child is obviously under weight, but his general demeanour is cheerful. Covering the whole nose is a large brownish crust, which can be periodically detached, its under-surface showing digitate processes, which extend into the underlying granulomatous area.

Perlèche is present and there are white membranous patches on the buccal mucous membrane. Externally the cheeks are pitted with the scars of healed pustules.

Four of the fingers show a uniform erythema of the two terminal phalanges. From three the nails have been lost and the fourth is in process of extrusion.

*Investigations.*—In December 1948 Dr. J. T. Duncan reported that skin scrapings from the right thumb, from the lip and nasal crust all yielded growths of *Candida albicans*.

No glycosuria.



FIG. 1.—Showing the nasal plaque and perlèche.

*Treatment.*—The tonsils have been removed and he has been receiving speech therapy for several years.

Many fungicides and antiseptics have been applied both to the buccal and the cutaneous lesions. Castellani's paint appeared effective for the fingers during one period and gentian violet certainly reduces the severity of the buccal condition. Various preparations of undecylenic acid ointments have been applied.

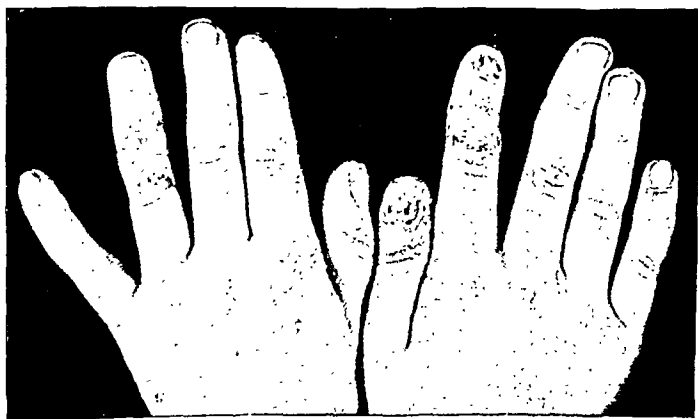


FIG. 2.—The fingers, at the stage when only the left ring finger and the right thumb and index finger were involved.

X-ray therapy was attempted for the paronychia. Potassium iodide was given but produced looseness of the bowels. A course of oidiomycin, prepared by Dr. Duncan, was used for several months, without any local or general reaction being produced. At present he is receiving injections of an autogenous vaccine, which causes some local swelling and tenderness.

*Progress.*—A fourth finger has become involved during the last three months, despite local and systemic treatment. The nasal lesion, however, is receding at the edges with undecylenic acid ointment.



**Dr. C. H. Whittle:** These cases are, I think, rare but I saw a similar case recently in a child aged 2 or 3, though the lesions were much less extensive. The disease began as thrush in the mouth, spread to the buttocks and subsequently developed on the right thumb, where it was attributed to thumb-sucking. The mother took measures to stop this, but a few weeks later the other thumb was similarly affected. Monilia were recovered without difficulty.

**Dr. G. C. Wells:** I think that this condition is a distinct entity, and differs from other kinds of moniliasis in being intractable. Such cases start in infancy with oral thrush, but infection persists and spreads to the skin around the mouth and nose, where eventually the lesions become granulomatous. Teeth and nails are usually affected.

Hauser and Rothman have recently recorded a severe example of this condition and discuss 8 cases in the literature, under the suggested designation of "Monilial Granuloma" (*Arch. Derm. Syph.*, to be published).

**Dr. W. N. Goldsmith:** In the cases mentioned by Dr. Wells, was monilia found repeatedly in different phases of the disease? I have in mind 2 similar cases, both in little girls, starting from early in life. The first was the little girl illustrated in figs. 437 and 438 of MacLeod's "Diseases of the Skin", 2nd edition (1933), showing a crusted, suppurative affection of eyelids, *alae nasi*, corners of the mouth, and nail-folds of fingers and toes. She had originally been seen by me, and we had cultured only *Staphylococcus pyogenes aureus*. Later, Dr. MacLeod cultivated *Monilia pinoyi*. Still later, she was under Sir Archibald Gray, who was unconvinced that it was moniliasis.

The second case was under me recently at University College Hospital. I first was asked to see her in early childhood, for warts around the vulva. She had a persistent vaginal discharge, for which no infective cause could be found. She also had suppurative, crusted blepharitis, and perionychia. The condition persisted for years, and we never found monilia. Gradually the eruption extended on to her limbs and trunk, in the form of lesions which became more and more unmistakably *psoriasis*.

Looking back now at MacLeod's fig. 438 of the first case, I am interested to see that there are well-defined plaques over the point of both elbows, and also on the extensor aspect of both knees.

These cases have been extremely unresponsive to treatment.

**Dr. R. T. Brain:** I suggest treatment internally with gentian violet capsules. It is also safe to use gentian violet intravenously, though it may give the patient a purplish hue for a few hours.

**Dr. G. C. Wells:** In the case of moniliasis that I mentioned *Candida albicans* was found in the scales consistently during many months' observation.

#### Superficial Amelanotic Melanocarcinoma or Precancerous Melanoma.—THERESA KINDLER, M.D.

The patient is 63 years old, in fairly good health. There is moderate hypothyroidism, controlled by treatment. W.R. is negative and blood-count and urine normal. The skin shows the end-stage of generalized vitiligo, resulting in almost complete loss of pigment except for pigmentation of neck and face and irregular symmetrical pigmented areas in the axillae and elbow flexures. There are multiple seborrhœic warts on her back and abdomen, and a warty black naevus under the left breast since childhood. She has one daughter who has multiple pigmented naevi. The patient states that nine years ago a red scaling spot developed in apparently normal skin near the left elbow and grew slowly by extension and confluence with adjoining satellite lesions.

**On examination.**—There is a psoriasiform red glistening scaling superficial plaque, 12 by 20 cm. in diameter, involving left elbow and adjoining parts of forearm. The area is enclosed by an irregular, smooth, firm, translucent, slightly raised border 2 to 3 mm. wide. In some parts of the lesion there are lighter patches and breaking up of borderline (fig. 1). These



FIG. 1.—Superficial amelanotic melanoma on left forearm. Light patches and broken border-line suggesting involution.

reaching to just above the wrists and wore his shirt-sleeves rolled up above the elbows. After three days of this work he developed soreness, redness and marked swelling of the forearms. He at once stopped work and was treated at U.C.H. Casualty Department with calamine lotion. The acute condition gradually subsided during the following two weeks, leaving a pigmentation of the skin which has persisted unchanged. According to the patient such a condition is unknown to regular workers in the trade.

*On examination.*—A young man with brown hair and a fresh complexion, apparently healthy apart from the skin lesions and a swelling of the right side of the face due to an alveolar abscess. The skin lesions are purplish-brown macules 1–2 mm. in diameter, forming a distinct band about 2 cm. wide, encircling each forearm about 5 cm. proximal to the wrist-joints and also scattered irregularly farther up the forearms, especially on the flexor aspects. Some of the macules are pierced centrally by hairs; some are distinctly depressed beneath the general surface of the skin and have a shiny atrophic appearance. Some are uniform; others consist of a central pale area with a peripheral ring of pigmentation. The intervening skin is normal. Old scars do not show pigmentation.

*Investigations.*—Hess test for capillary fragility negative. Full blood-counts normal. Bleeding and clotting times normal.

This case is presented as one of curious pigmentation of the skin following an acute inflammation caused, apparently, by chafing and contact with rubber, hydrochloric acid and metallic salts. The appearance suggested petechiæ, but the condition has been unchanged for over three weeks and there is no evidence, physical or hæmatological, of a general purpuric state at present. It is tempting to try to relate the distribution of the macules to that of the hair-follicles. Is it possible that the noxa entered the follicles and caused a disturbance at a deeper level than in the intervening skin which has healed without trace? It is hoped to establish the nature of the pigment on biopsy, bearing in mind the possibility of a deposit of metallic compounds from the "pickling" fluid.

**Dr. W. N. Goldsmith:** I had not seen anything at all resembling this before, following exogenous dermatitis, and, as Dr. Hare has said, the condition is said to be unknown among regular workers in "pickling" metal.

**The President:** The one fleeting glance I had at it suggested a resemblance to the case which Dr. P. D. Samman showed at the last meeting. The histology will perhaps settle the question.

**Dr. R. M. B. MacKenna:** The condition seems to have occurred above the glove level—the exact reverse of the cases published in America among negroes in which a condition of this kind followed upon the wearing of gloves.

**POSTSCRIPT (November 1949).** **Dr. Hare:** *Histology:* In the upper corium there are deposits of granular pigment which stain dark blue with Perl's method. These granules are mainly extracellular but a few lie in macrophages. They are seen in two sites: (a) Around the upper ends of the hair follicles; (b) in an area of fibrosis underlying the only abnormal part of the epidermis seen in the sections prepared. Here there is a gap in the whole depth of the epidermis, plugged with a hyaline acidophil material.

The iron pigment does not lie in striking relation to the blood-vessels. No extravasated red blood corpuscles are seen. There is no apparent abnormality of the melanin pigmentation.

I think the histological findings answer the points raised by Dr. Wigley and Dr. MacKenna. It is hoped to report this case more fully in the *British Journal of Dermatology*.

The following cases were also shown:

**Mycosis Fungoides.**—Dr. HUGH GORDON.

**Leprosy.**—Dr. D. E. OAKLEY.

**? Poikiloderma-Jacobi or Mycosis Fungoides or Parapsoriasis en Plaques in Male of 75.**—Dr. STEPHEN GOLD.

**Scleroderma.**—Dr. BENTLEY PHILLIPS.

**Adenoma Sebaceum and Periungual Angiofibromata.**—Dr. ARTHUR ROOK.

**Lichen Sclerosus et Atrophicus.**—Dr. F. J. JENNER.

**Circumscribed Scleroderma with Morphea Guttata and Pigmentation.**—Dr. BETHEL SOLOMONS, Jr.

(These cases may be published later in the *British Journal of Dermatology*.)

# PROCEEDINGS *of the* ROYAL SOCIETY OF MEDICINE

ISSUED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE

HONORARY EDITORS

ERIC A. CROOK

E. R. CULLINAN

EDITOR

J. M. BROWNE KUTSCHBACH

G. S. W. ORGANE (Anæsthetics)

J. S. RICHARDSON (Clinical)

J. B. BROOKSBY (Comparative Medicine)

E. W. PROSSER THOMAS (Dermatology)

E. F. SCOWEN (Endocrinology)

ALLAN McFARLAN (Epidem. & State Med.)

A. C. WHITE (Exper. Med. & Therap.)

I. E. McCracken (History of Medicine)

W. A. MILL (Laryngology)

MAURICE DAVIDSON (Medicine)

J. St. C. ELKINGTON (Neurology)

LESLIE WILLIAMS (Obstetrics & Gynæcology)

B. W. FICKLING (Odontology)

F. T. RIDLEY (Ophthalmology)

H. L.-C. WOOD (Orthopædics)

C. S. HALLPIKE (Otology)

A. G. SIGNY (Pædiatrics)

F. R. SELBIE (Pathology)

M. B. RAY (Physical Medicine)

O. V. LLOYD-DAVIES (Proctology)

DENIS HILL (Psychiatry)

F. CAMPBELL GOLDING (Radiology)

CHARLES DONALD (Surgery)

G. M. FINDLAY (United Services)

A. CLIFFORD MORSON (Urology)

SECRETARY OF THE ROYAL SOCIETY OF MEDICINE

G. R. EDWARDS



# MALE HORMONE

ROUSSEL

---

**TAB. METHYLTESTOSTERON. B.P.**

Glosso-Sterandryl—5, 10 and 25 mg.

**INJ. TESTOSTERON. PROP. B.P.**

Sterandryl—5, 10, 25, 50 and 100 mg.

**IMPLANT** of 100 mg. TESTOSTERONE  
Sterandryl—Implant.



ROUSSEL LABORATORIES LIMITED  
4, Golden Square, London, W.1      GERard 3111-2

# PROCEEDINGS

## OF THE

# ROYAL SOCIETY OF MEDICINE

Vol. XLII    No. 12    December 1949

## CONTENTS

Whole  
Proceedings  
Page

### Section of Endocrinology

#### JOINT MEETING WITH THE SOCIETY FOR ENDOCRINOLOGY

|                                                                                                                                         |     |
|-----------------------------------------------------------------------------------------------------------------------------------------|-----|
| Autoradiographs with Radio-active Iodine.—I. DONIACH, M.D., and S. R. PELC, Ph.D.                                                       | 957 |
| The Thyroid Clearance Rate of Plasma Iodine as a Measure of Thyroid Activity.—<br>N. B. MYANT, B.M., and E. E. POCHIN, M.D., F.R.C.P... | 959 |
| Urinary Excretion of Radio-active Iodine as a Measure of Thyroid Activity.—<br>A. STUART MASON, M.B., M.R.C.P.                          | 961 |
| Clinical Use of Radio-active Iodine.—RUSSELL FRASER, M.D., F.R.C.P...                                                                   | 962 |

### United Services Section

|                                                                                             |     |
|---------------------------------------------------------------------------------------------|-----|
| DISCUSSION: THE PROFESSIONAL FUTURE OF MEDICAL OFFICERS OF THE FIGHTING FORCES<br>[Summary] | 969 |
|---------------------------------------------------------------------------------------------|-----|

### Section of Laryngology

|                        |     |
|------------------------|-----|
| STENOSIS OF THE LARYNX | 981 |
|------------------------|-----|

### Section of Urology

|                                             |     |
|---------------------------------------------|-----|
| DISCUSSION ON CHRONIC RETENTION OF URINE... | 987 |
|---------------------------------------------|-----|

### Section of Proctology

|                                      |      |
|--------------------------------------|------|
| DISCUSSION ON PROLAPSE OF THE RECTUM | 1005 |
|--------------------------------------|------|

### Section of Ophthalmology

|                                                                                          |      |
|------------------------------------------------------------------------------------------|------|
| Optic Nerve Compression and its Differential Diagnosis.—S. P. MEADOWS, M.D.,<br>F.R.C.P. | 1017 |
|------------------------------------------------------------------------------------------|------|

### Section of Medicine

|                                                                          |      |
|--------------------------------------------------------------------------|------|
| March 22, 1949                                                           |      |
| DISCUSSION: SPECIALIZATION—ITS VALUE AND ABUSE                           | 1035 |
| April 26, 1949                                                           |      |
| DISCUSSION ON NON-TUBERCULOUS CONDITIONS REVEALED BY MASS RADIOGRAPHY... | 1039 |

All communications concerning Editorial Business should be addressed to  
THE HONORARY EDITORS, 1, WIMPOLE STREET, LONDON, W.1

*Applications for advertisement space in the "Proceedings" should be made to the Society's official advertising agents Messrs. C. Mitchell & Co. Ltd., Mitchell House 1 and 2, Snow Hill, London, E.C.1.*

Copies of the whole *Proceedings* may be purchased through any bookseller. Prices are as follows:—

|                                                                     |                           |
|---------------------------------------------------------------------|---------------------------|
| Single copies .. .. .                                               | 10s. 6d. each, post free. |
| Annual subscription, covering 12 monthly issues and annual index .. | £6 6s. 0d.                |

Reprints of Sectional parts may be obtained direct from the Society. Prices are as follows:—

|                             |                          |
|-----------------------------|--------------------------|
| Single copies .. .. .       | 3s. 6d. each, post free. |
| Annual subscription .. .. . | 15s. 0d.                 |

Fellows and Members of the Royal Society of Medicine are asked to apply direct to the Society for any copies of the *Proceedings* they may require, whether whole or Sectional, in addition to those they receive *gratis*. Prices are as follows:—

**Whole *Proceedings*:**

|                                                            |                          |
|------------------------------------------------------------|--------------------------|
| Single copies .. .. .                                      | 7s. 6d. each, post free. |
| Complete volume (12 monthly issues and annual index) .. .. | £5 0s. 0d.               |

**Sectional *Proceedings*:**

|                             |                          |
|-----------------------------|--------------------------|
| Single copies .. .. .       | 3s. 0d. each, post free. |
| Annual subscription .. .. . | 10s. 0d.                 |

## Publication Rules.

**Copyright:** The Society holds the copyright of all matter accepted for publication in the *Proceedings*. Requests for subsequent publication elsewhere should be made to the Honorary Editors. All papers, &c., presented at meetings (other than those which have been previously published) are held to be subject to the Society's copyright until a decision in regard to their publication has been made.

**Digests:** Requests for permission to make Digests from the *Proceedings* should be addressed to the Honorary Editors.

**Manuscripts** should be concise and *carefully revised for press*. They must be top copies, typewritten in double spacing, with the author's name, degrees and address on the first page. A carbon copy should be retained by the author.

The text must contain references to all tables and illustrations; these should be numbered and packed separately.

Dosages and other measurements should be given in metric units.

**References:** The Harvard system should be followed, i.e. each work should be cited in the text by the author's name and date of publication, and at the end of the paper a list should be given in alphabetical order according to the authors' names. Names of journals should be abbreviated in accordance with the "World List of Scientific Periodicals", e.g.

ATKINSON, J. (1921) *J. biol. Chem.*, 47, 134.

With the title of a book the place of publication should be given.

**Illustrations** should be numbered consecutively and the top clearly marked. They must be suitable for direct photographic reproduction.

Photographs should be glossy prints. *No negatives or slides will be accepted*. The important feature of each photograph should be indicated, preferably by pencil lines on the back.

All numerals, &c., appearing on diagrams should be large and bold to allow of reduction in size.

**Blocks** used for the illustration of articles in the *Proceedings* will be presented to authors shortly after each volume is concluded.

**Reprints and Excerpts** may be obtained from the Society's printers, Messrs. Staples Press Limited, 83-91, Great Titchfield Street, London, W.1.

## Section of Endocrinology

President—H. GARDINER-HILL, M.B.E., M.D., F.R.C.P.

[May 25, 1949]

JOINT MEETING WITH THE SOCIETY FOR ENDOCRINOLOGY  
MORNING SESSION

### Autoradiographs with Radio-active Iodine

By I. DONIACH, M.D., and S. R. PELC, Ph.D.

DURING the past two years we have developed the stripping film technique for making autoradiographs first described by Pelc in 1947, which method is fully discussed elsewhere (Doniach and Pelc, 1949). We worked chiefly with rats, giving them carrier free  $I^{131}$  by subcutaneous or intraperitoneal injections in doses of 5 to 50 microcuries. Recently we have found that as small a dose as 0.02 microcurie, when the animal is killed nineteen hours after injection, will suffice. The concentration of  $I^{131}$  resulting from this administration is



FIG. 1.



FIG. 2.

FIG. 1.—Hæmalum-stained autoradiograph of thyroid of rat killed two and a half hours after a subcutaneous dose of 15 microcuries  $I^{131}$ . Varying concentrations of blackened photographic grains overlie the colloid of different follicles.

FIG. 2.—Unstained autoradiograph of thyroid of rat killed ten minutes after a subcutaneous dose of 50 microcuries  $I^{131}$ . Widespread uptake of iodine into the follicular colloid is already seen.

0.27 microcurie per gramme of thyroid tissue. The final preparation consists of a  $5\mu$  section of thyroid mounted on a glass slide and covered by a closely attached strip of developed photographic emulsion 2 to  $3\mu$  thick. Concentrations of blackened photographic grains indicate the presence of radio-active material in the underlying tissue, the resolving power being 2 to  $3\mu$ . The slide can be viewed unstained under the microscope with the condenser racked down (figs. 2 and 3) or through the phase contrast microscope (fig. 4). The sections can be stained with a hot carbol fuchsin neutral red mixture before applying the film or with hæmalum after photographic processing. Fig. 1 shows a hæmalum-stained autoradiograph of the thyroid of a rat killed two and a half hours after receiving a subcutaneous injection

of 15 microcuries of  $I^{131}$ . The preparation was left in the dark (exposure time) for seven days before photographic development.

Experiments in which rats were killed at varying time intervals showed iodine uptake into the follicular colloid within ten minutes of receiving the injection (fig. 2). By two and a half hours (fig. 1) increased iodine uptake produced a more intense autoradiograph and though all follicles contained radio-active iodine, concentration was greater in the centre than in the periphery of the gland. The iodine was presumably in an organically bound form since it had not been removed from the tissue by fixation and dehydration in ethyl alcohol. Similar findings were described by Leblond and Gross (1948). By forty-eight hours (fig. 3) iodine had disappeared from many central follicles though still present in the peripheral ones. Autoradiographs made at four, seven and nine days confirmed the much more rapid turnover in the central as compared with the peripheral follicles. The thyroid glands of rats given thiouracil before or together with radio-active iodine failed to produce autoradiographs.

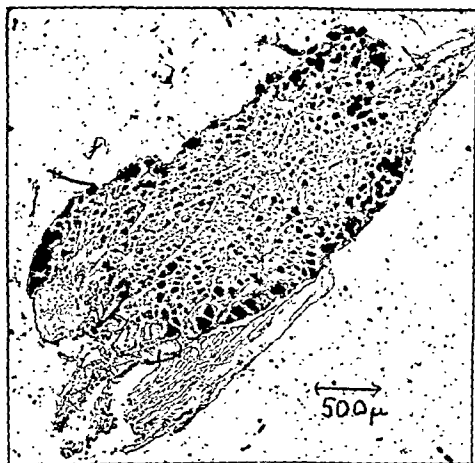


FIG. 3.



FIG. 4.

FIG. 3.—Unstained autoradiograph of thyroid of rat killed forty-eight hours after a subcutaneous dose of 10 microcuries  $I^{131}$ . Both intensely blackened and empty follicles are seen in the centre whereas most of the peripheral follicles still contain radio-active iodine.

FIG. 4.—Unstained autoradiograph of rat thyroid; phase contrast below, no phase plate above. The rat was given daily injections of 20  $\mu$ g. dL thyroxine for six weeks and then 2 injections of thyrotrophic hormone followed by 30 microcuries  $I^{131}$ . It was killed one hour after receiving the  $I^{131}$ . The iodine is distributed mostly in rings, seen by phase contrast to be concentrated in the follicular epithelium rather than the colloid.

Leblond and Gross (1948) found that in rats either pretreated with non-radio-active iodine or hypophysectomized, thyroid autoradiographs made one hour after injection of  $I^{131}$  showed iodine mostly within the cells rather than the colloid. The follicles were outlined as rings. We were able to reproduce this effect by pretreatment of rats with daily injections for six weeks of an alkaline solution of 20  $\mu$ g. of dL-sodium thyroxine. This treatment presumably damped down the pituitary production of thyrotrophic hormone (Griesbach and Purves, 1943), producing a selective functional hypophysectomy. We then hoped that a few days' administration of a preparation of thyrotrophic hormone to thyroxine-treated rats might re-establish a normal deposition of iodine into the colloid. However, in the doses we used, it only intensified the ring effect of cellular rather than colloid uptake of iodine (fig. 4).

We have to date made a few autoradiographs of human thyroids. These were successful, provided the patients had had no previous iodine therapy. Administration of 20 to 100 microcuries of  $I^{131}$  by mouth twenty-four to forty-eight hours before thyroidectomy proved adequate.



We wish to thank Mr. H. C. Toghill for his technical assistance and Mr. E. V. Wilmott, F.R.P.S., for preparing the photomicrographs of figs. 2 and 3.

## REFERENCES

- DONIACH, I., and PELC, S. R. (1949) *Brit. J. Radiol.* (In the press.)  
 GRIESBACH, W. E., and PURVES, H. D. (1943) *Brit. J. exp. Path.*, 24, 185.  
 LEBLOND, C. P., and GROSS, J. (1948) *Endocrinology*, 43, 306.  
 PELC, S. R. (1947) *Nature*, 160, 749.

## The Thyroid Clearance Rate of Plasma Iodine as a Measure of Thyroid Activity

By N. B. MYANT, B.M., and E. E. POCHIN, M.D., F.R.C.P.<sup>1</sup>

In the following account of the uptake of radio-iodine by the human thyroid, we wish to describe certain quantitative measures of the rate of uptake, and to discuss their clinical application. Doses of 30 microcuries of  $I^{131}$  have been used, either with no carrier or with 20-microgram amounts of inert iodine. Such doses have been given as iodide either orally or intravenously to normal and thyrotoxic subjects. We have followed the urinary excretion and plasma concentration by conventional liquid counting methods, and have differentiated labelled iodide from thyroxine in the plasma by Taurog and Chaikoff's butanol extraction against alkali. The thyroid uptake of the dose has been determined using a gamma counter opposite the neck with accurate positioning of neck and counter, radiation from the rest

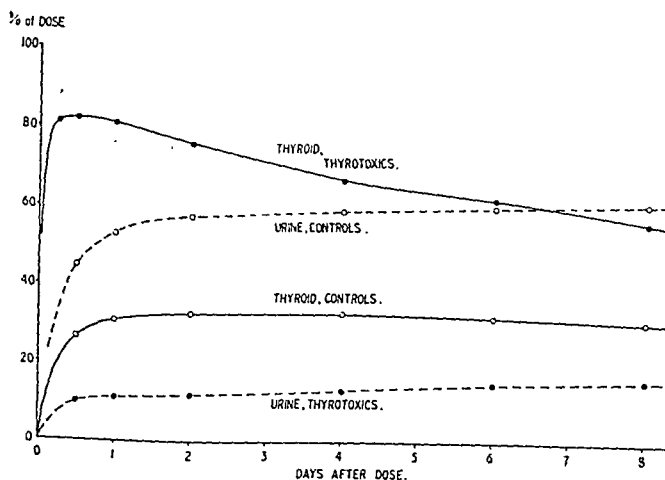


FIG. 1.—Mean values for thyroid and urine content of radio-iodine in groups of normal and thyrotoxic subjects.

of the body being screened by a lead shield [1]. In calculating the radio-iodine content of the gland from the counting rate opposite to it, it is necessary to know both the position of the thyroid and the contribution that scattered radiations make to the count. The former can be quite accurately estimated by making counts with the counter at different distances from the neck, since the counting rate falls off inversely with the square of the separation between counter and source, and thereby reveals the position of the source [2]. The effect of scattered radiations has been determined in separate experiments in which a known dose has been introduced into the neck at the thyroid level in a swallowed Ryle's tube. The observed counting rate from the swallowed tube is compared with that from the same tube hung in air at an equal distance from the counter, and radiations scattered from neck tissues are thereby found to increase the count by about 27%.

In this way, one can determine the percentage of a dose in the thyroid and in the urine, and its concentration in plasma at any interval after its administration. Fig. 1 shows that, as an average of a group of normal subjects, the thyroid continues to take up iodine for two

<sup>1</sup>Work undertaken on behalf of the Medical Research Council.

or three days, reaches a peak content of about 33% of the dose, when its content starts to fall slowly. In a group of untreated thyrotoxic subjects, the maximum uptake was greater, was reached earlier, and the iodine was lost more rapidly in the ensuing days. In each group, the urinary changes correspond, an initial stage of rapid excretion being complete in about two days in normal subjects when 60% of the dose has been excreted, excretion continuing at a slow rate thereafter. In thyrotoxics, the initial stage is complete earlier, accounts for a much smaller percentage of the dose, and is followed by a rather faster rate of subsequent excretion.

The plasma concentration of radio-iodine (fig. 2) also reflects the same time scales. In

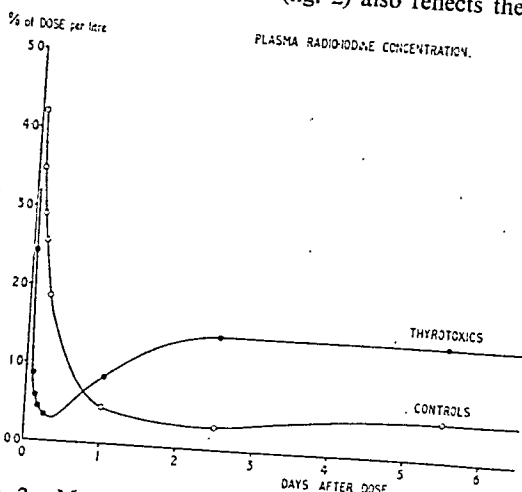


FIG. 2.—Mean values of plasma radio-iodine concentration in groups of normal and thyrotoxic subjects.

normal subjects it falls to a low value in two days, during which time the butanol fractionation shows the activity to be due to iodide. The concentration then rises again slowly, and the activity is now found in the thyroxine fraction, where it has been detected at two days, but not earlier, after the dose. In thyrotoxic patients, the iodide fall is more rapid, and the thyroxine rise earlier and greater, and radio-thyroxine has been demonstrated in the plasma as early as three hours after the dose, and is commonly present by seven hours. The following notes deal only with the uptake phase during the first hours after the dose, and before output of radio-thyroxine from the thyroid has appreciably started.

It will be noted that in the thyrotoxic as well as in the normal group, equal times are required for completion of thyroid uptake, of the initial urinary excretion and of the removal of radio-iodide from the plasma. Moreover, when the curves are compared in individual subjects, it is found that the rate of rise of the thyroid count is directly proportional to the plasma radio-iodide concentrations at the time. And similarly, the rate of urinary excretion runs proportional to the plasma concentration [1]. This is perhaps an expected result since the body does not distinguish radio-iodine from normal iodine, and the thyroid and kidneys proceed to remove iodide from the plasma at a steady rate regardless of the administration of a test dose of radio-iodide. One may say then that the thyroid is clearing a constant volume of plasma each minute of its contained iodide, and the test dose merely enables us to determine what volume of plasma is so cleared. If, for example, the thyroid is taking up radio-iodine at a rate of 5% of the dose per hour at a time when the plasma contains 5% of the dose per litre, it may be said that the thyroid is clearing 1 litre of plasma per hour of its iodide. As with the conventional renal clearance, this gives a valuable index of the thyroid activity. The renal clearance rate for iodide is determined similarly by the ratio between the rate of urinary excretion of radio-iodide and its plasma concentration at the time.

In practice the determination of clearance rates requires certain precautions. If the determination is made too early after an oral dose, the rise in counting rate opposite the neck is due partly to a rising iodide content of neck muscles. After an hour, however, this content is about constant, as judged from parallel counts over the thigh, and so does not contribute to the speed of rise of the neck counting rate. Again, if the clearance is determined so late that appreciable labelled thyroxine is being discharged from the gland, the plasma radio-activity does not measure only radio-iodide, and the rise of neck count does not measure uptake only, so that low values of the clearance are obtained. The test is still in this sense

experimental, and we prefer to base a value on several plasma samples. Valid readings are, however, obtained between one and two hours after an oral dose given several hours after food. And if an intravenous dose is used, the patient can come up as an outpatient at any convenient time and the test be completed with little more than an hour's work.

In subjects without thyroid disease, thyroid clearance rates have lain between 5 and 40 ml. of plasma cleared of their iodide per minute, averaging 25 ml./min. In 15 subjects with clear thyrotoxicosis, values have always exceeded 100 ml./min. and usually exceed 150. The clearance in myxoedema has been a few ml./min. only, and its value in non-toxic goitre has been normal or a little raised, one value of 60 having been observed. The renal clearance for iodide has averaged 30 ml./min., and is unchanged in thyrotoxicosis.

Since at all times the thyroid and kidneys are taking up iodide in proportion to their clearance rates, the amounts in thyroid and urine at the end of the uptake phase should approximately measure the ratio of these rates. After twenty-four hours, most of the dose is in fact shared between thyroid and urine in about this ratio, the amount in the tissues being under 10% except in cases of thyrotoxicosis with rapid output from the thyroid. The urinary excretion by twenty-four hours is then a rough measure of the ratio between renal clearance and the combined renal and thyroid clearance. It affords therefore an easily determined index which is influenced by the thyroid clearance. Unfortunately, the renal clearance for iodide varies widely in normal subjects and also influences the 24-hour output of the dose, and the effects of a high thyroid clearance may be simulated by a low renal clearance. It is probably for this reason that the values from the urinary excretion test in normal and thyrotoxic subjects may overlap. This overlap could be reduced if the renal clearance were also determined, as may be done by liquid counter methods alone, but the test would then become inconveniently long, and certain other indices of differing accuracy and simplicity might be suggested. These vary in the directness with which they estimate thyroid clearance, and therefore in the crispness with which they separate normal from increased thyroid uptake of iodide. For example, a simple comparison of the counting rate opposite the neck to that opposite the thigh at one hour after the dose appears to separate the groups well and the ratio correlates closely with the thyroid clearance. As an even simpler test, the plasma radio-iodide concentration two hours after an oral or intravenous dose promises to separate the groups cleanly and it would be simple to give the dose to an outpatient, orally and several hours after food, with instructions that she return for a blood sample two hours later. The plasma could then be compared in a liquid counter with a standard containing 2% of the dose per litre, since the normal values have been above, and those in thyrotoxicosis below, this figure. If a simple clinical test were required a number of patients could be examined in this way within an hour. For any closer analysis of the degree of thyroid overactivity in taking up iodide, the rather more complex but more direct index of thyroid clearance rate appears to be preferable, and seems likely to be of value in the analysis both of thyroid physiology and disease.

#### REFERENCES

- 1 MYANT, N. B., POCHIN, E. E., and [the late] GOLDIE, E. A. G. (1949) *Clin. Sci.*, 8, 109.
- 2 —, HONOUR, A. J., and POCHIN, E. E. (1949) *Clin. Sci.*, 8, 135.

## Urinary Excretion of Radio-active Iodine as a Measure of Thyroid Activity<sup>1</sup>

By A. STUART MASON, M.B., M.R.C.P.

THE measurement of urinary excretion of radio-active iodine is a simple procedure involving no disturbance of the patient and the minimum of apparatus. Moreover, only small doses of the isotope are required. Dr. Pochin has shown that the proportion of a dose of  $I^{131}$  excreted in the urine varies inversely with thyroid function, but urinary values alone will not give such an exact picture of thyroid function as the iodine clearance rate.

The present investigation was to determine whether the measurement of urinary radio-iodine could be used as a routine diagnostic measure in thyroid disease. After preliminary trials a dose of 10  $\mu$ c. of  $I^{131}$  was found suitable. About 50 gamma of sodium iodide was added as carrier. The radio-activity of urine samples was measured with a glass liquid counter described by Veall, in conjunction with a conventional scaling and quenching unit, and expressed as a percentage of the dose administered.

A comparison of the twenty-four-hour excretion of  $I^{131}$  in urine was made in 49 patients, in whom clinical evidence indicated normal, increased, or decreased thyroid function.

<sup>1</sup> A fuller presentation of this subject has appeared in the *Lancet* (1949) ii, 456.

In 26 normal subjects, the amount excreted varied from 28% to 72% as compared with 5% to 26% in 19 cases of thyrotoxicosis. In 4 cases of myxœdema the values were within the normal range. A more satisfactory separation was obtained by subdividing the twenty-four-hour period of collection. The excretion of  $I^{131}$  in the first six hours following the tracer dose is not markedly different in the three groups, but the subsequent period from six to twenty-four hours shows an obvious difference. In this period the excretion in normals varied from 10% to 25% while the highest amount excreted by the mildest case of thyrotoxicosis was 4.5%, the average case excreting under 2%. The difference is not so marked in myxœdema, the values lying between 26% to 33%.

On further analysis it was found that, in general, the summed excretion plotted against time approximated to an exponential form, and a mean exponential could be drawn through the actual values. This confirmed Keating's findings, and his method of calculating an index of thyroid iodine collection was then employed.

The thyroid rates in the groups already discussed were as follows. Normal: 0.055 to 0.10. Thyrotoxicosis: 0.28 to 1.18. Myxœdema: 0.005 to 0.04. The more severe the thyrotoxicosis the higher was the thyroid rate, and the rate for the mildest case was over three times the mean normal. Thus the six to twenty-four-hour bulk excretion proved an adequate diagnostic aid, while the thyroid rate gave a more exact picture of the degree of thyroid dysfunction. Investigations were also done in a group of 7 patients in whom clinical observation (including B.M.R.) led to a diagnosis of mild hyperthyroidism insufficient to justify antithyroid therapy. Both the six to twenty-four-hour excretion and thyroid rate in this group fell between the limits of normal and thyrotoxicosis. It seems that such cases represent an intermediate grade of thyroid over-activity, between normal and clinical thyrotoxicosis.

The two most important possibilities of error in assessing thyroid function from urinary excretion of  $I^{131}$  are failure of renal function, and previous administration of iodine. Four patients with renal failure showed a diminished excretion of the tracer dose (12% to 26% in twenty-four hours) which might give rise to an erroneous impression of thyrotoxicosis. The thyroid rate in these cases was normal, demonstrating that Keating's analysis gives a reasonable correction for changes in renal function. Administration of iodine increases the excretion of  $I^{131}$ . In one case of thyrotoxicosis, treated with iodide for three weeks, excretion values were normal although signs of thyrotoxicosis were still manifest. Clearly, it is important to be sure that no iodine has been given in any form prior to a diagnostic test with  $I^{131}$  and the amount of carrier iodine given with the tracer dose must be kept very low. In this series there was no control of dietary iodine, and it may well be that the variation in excretion of radio-active iodine among normal subjects is partially explained by differences in previous iodine intake. It is noticeable that the average twenty-four-hour excretion for each group in this series is less than that reported for similar groups studied in U.S.A. Again, differences in dietary iodine may explain the discrepancy.

Bearing in mind the limitations of the method, and the fact that it is not a direct measurement of thyroid iodine uptake, the urinary excretion of a dose of  $I^{131}$  is a simple and useful diagnostic aid in determining thyroid activity. Bulk samples from six to twenty-four hours after the dose give a clear-cut separation between the normal and the thyrotoxic patient, while Keating's more involved calculations produce a closer assessment of the degree of hyperfunction. In myxœdema this calculation is of diagnostic use but requires further study, with collection of urine over a forty-eight-hour period.

#### REFERENCE

KEATING, F. R., *et al.* (1947) *J. clin. Invest.*, 26, 1138.

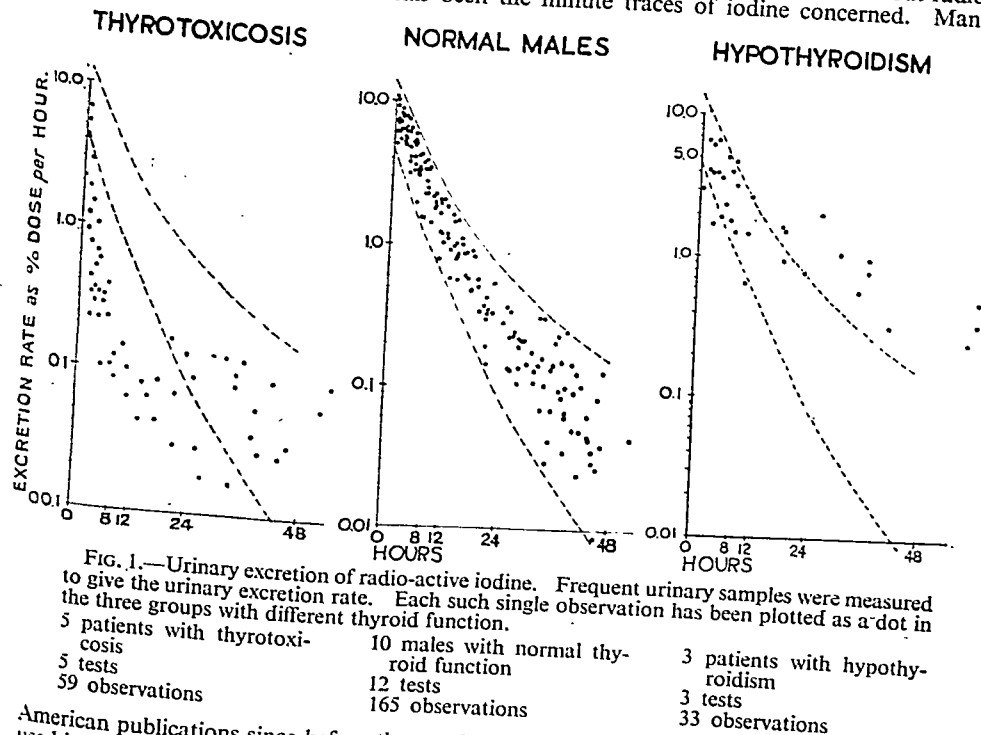
### Clinical Use of Radio-active Iodine

By RUSSELL FRASER, M.D., F.R.C.P.

MUCH has already been published to indicate the potential usefulness of  $I^{131}$  for radiotherapy either of thyroid cancer or of hyperthyroidism. As might be expected, the immature malignant thyroid cell often (60-90%) does not take up iodine. But the great usefulness of radio-active iodine in those cancers which do, can be readily imagined; and some success has even been achieved in stimulating malignant secondaries which did not originally take up iodine to do so. The use of radio-active iodine, or of other forms of radiation, in the treatment of thyrotoxicosis has, however, little to commend it except in the rare cases for whom other treatments are not practicable or have repeatedly failed. For these cases it probably has much to commend it. But we have had experience mostly with the possible diagnostic use of radio-active iodine.

There are two potential diagnostic uses for  $I^{131}$ : (a) the recognition of thyroid under- or over-activity, and (b) the recognition of iodine uptake by tumours to indicate either their nature or their treatability by radio-active iodine. In such tests the radiation hazard must be borne in mind because the long-term carcinogenic risks are not yet fully known. The thyroid receives by far the most intensive radiation in such a test and only here need the dosage of  $I^{131}$  be even considered as a hazard. The dosage which we have used in the diagnostic test,  $10 \mu\text{c.}$  of  $I^{131}$ , may be estimated to deliver to a normal thyroid about 30 r; this is about equivalent to the skin radiation in a barium meal. But  $100 \mu\text{c.}$  delivering ten times this dose has been used by several workers in such a test; and we feel that this intensity of radiation should not be used on younger patients without some special diagnostic indications.

The fully developed and typical pictures of thyroid over-activity and under-activity are readily recognized by any experienced clinician; but not so the lesser degrees of abnormality. Thyrotoxicosis may often be indistinguishable from other diseases, such as, particularly, a neurosis or a primarily cardiac arrhythmia or failure; and various vague states of ill-health may raise the suspicion of hypothyroidism. Some useful screening tests have been developed in response to this need; notably the estimation of the B.M.R., the estimation of blood cholesterol for suspected myxoedema, and the observation of the response to iodides, thiouracil or to thyroid extract. But they are unreliable in the demonstration of thyroid dysfunction which is not severe enough to be obvious without their aid. It has, of course, long been hoped that measurement of iodine metabolism might supply the required test; but without radio-active iodine the limiting factor has been the minute traces of iodine concerned. Many



American publications since before the war have made clear that radio-active iodine can be used in patients to assess thyroid function. As we have used only urinary measurements and these seem to have a potential practical application already, the following remarks will be concerned with this urinary test. As mentioned, this method requires only  $10 \mu\text{c.}$   $I^{131}$ —a clearly safe dose; its accuracy is that of the urinary collection.

Fig. 1 shows the results of frequent measurements of the urinary excretion rate of  $I^{131}$  among a group of normals for forty-eight hours after administering the dose; each point shows the percentage of the administered dose excreted per hour at the plotted time. It will be seen that there is a definable range of normal distinguishable from that of a group of typical thyrotoxic patients and also from three typical hypothyroid patients.

From the above it is evident that the thyrotoxic rate is most different from the normal at 8–12 hours and the myxoedema rate most different at 24–48 hours. Thus it would appear that a sensitive simple indirect index of thyroid function would be obtainable from measuring

the radio-activity in four pooled samples: 0-8 hours, 8-12, 12-24 and 24-48 hours. The adequacy of the urinary collection can be checked by concurrent creatinine estimations and also by assessing the uniformity of the excretion trend in the four samples. With this simplified test we have found complete and reliable separation from our normal group of all the typical cases of thyrotoxicosis and myxœdema; the mean excretion at 8-12 hours of the thyrotoxic group is one-tenth of the normal, and that of the three myxœdema cases at 24-48 hours five times the normal. This may be compared in sensitivity with the B.M.R.—an average B.M.R. of 1,000% for a group of typical thyrotoxic cases and of -80% for a group of typical hypothyroids. Keating has suggested an analysis of the curve obtained by plotting the accumulation of  $I^{131}$  in the urine which gives a figure for thyroid activity. Unfortunately, this cannot be done simply without introducing considerable error and we have found that it adds no clinical advantage to the above procedure.

Other publications are all agreed that radio-active iodine can be used to distinguish typical thyrotoxicosis or myxœdema from the normal, but it is still unclear whether it is useful in diagnosing the doubtful case.

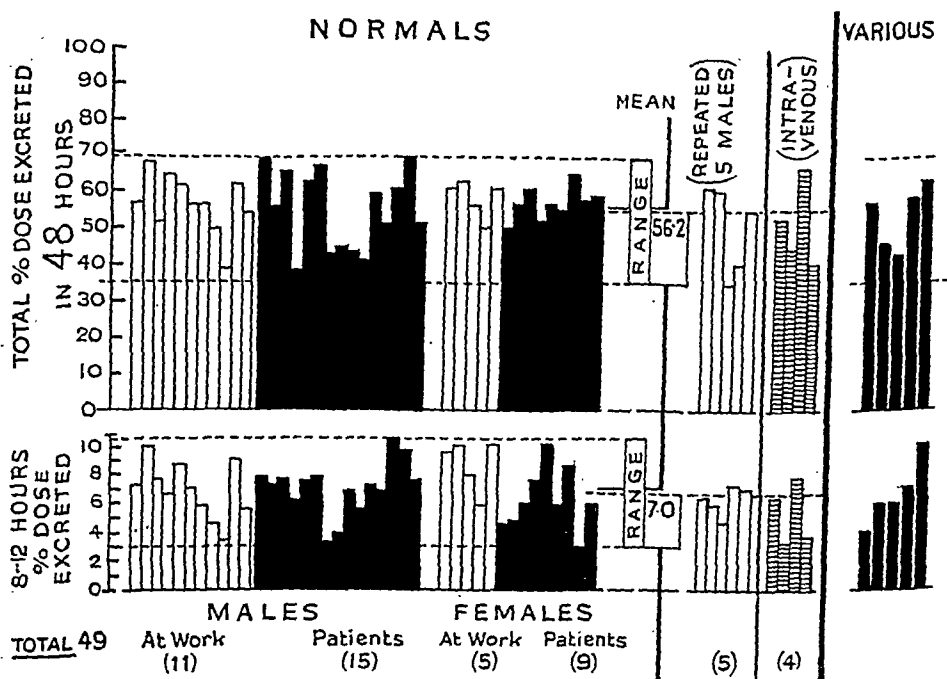


FIG. 2.—Radio-active iodine test results among normals and a few non-thyroid diseases, shown as in fig. 3. (Oral dose: 10  $\gamma$  pot. iodide 10-100  $\mu$ c.  $I^{131}$ .)

"Various" cases comprised: 1 retarded growth, 1 subacute nephritis, 1 craniopharyngioma with obesity, 1 anorexia nervosa and 1 phœochromocytoma (left to right).

(a) *Probably non-thyroid disease.*—Our normal groups used to establish the normal range have included, as well as normal active persons, a variety of bed patients without any suspicions of thyroid, renal or heart disease (fig. 2). Values outside this normal range are therefore unlikely to occur from the range of diet variation likely to be encountered in the London area, or from moderate variation in age or muscular activity.

We are at present investigating the extent to which excretion abnormalities may be encountered in the presence of œdema, and cardiac or renal defect. We have at present indications that renal defects unassociated with uræmia and quite extensive nephrotic œdema or cardiac failure do not usually give results outside the normal range. Œdema in the process of being discharged will probably influence the result; but such cases need only be studied in a steady state. No abnormal results have yet been encountered without evidence of thyroid disease, when cases of renal failure with uræmia are excluded. But further evidence is being collected, and this is only a preliminary indication. The effect of pregnancy has not yet been assessed.

(b) *Thyroid enlargement without clinical evidence of dysfunction—i.e. carcinoma and clinically non-toxic goitre.*

In the majority of such cases which we have tested, normal results have been found; three cases of malignant thyroid have been tested, including one secondary involvement of the thyroid by hypernephroma, and five cases of clinically non-toxic goitre. We have tested one case of acute thyroiditis and obtained a result typical of hypothyroidism; a result which was probably a correct assessment of the activity of the patient's thyroid cells, though there was no evidence of lack of circulating hormone. The signs of thyroiditis have now completely subsided and a retest is planned. No cases of chronic thyroiditis have been tested.

Only two abnormal test results were found from cases who appeared clinically to be non-toxic thyroid adenomas; the test results suggested thyrotoxicosis and deserve close scrutiny. The abnormal findings in the first case may have been due to a real mild thyrotoxicosis; or they may have been due to her being pregnant—we are not familiar with the range of values to be encountered in pregnancy<sup>1</sup>. An abnormally avid uptake by one patient at the same stage of pregnancy is reported by Chapman *et al.* (1948) without any comment

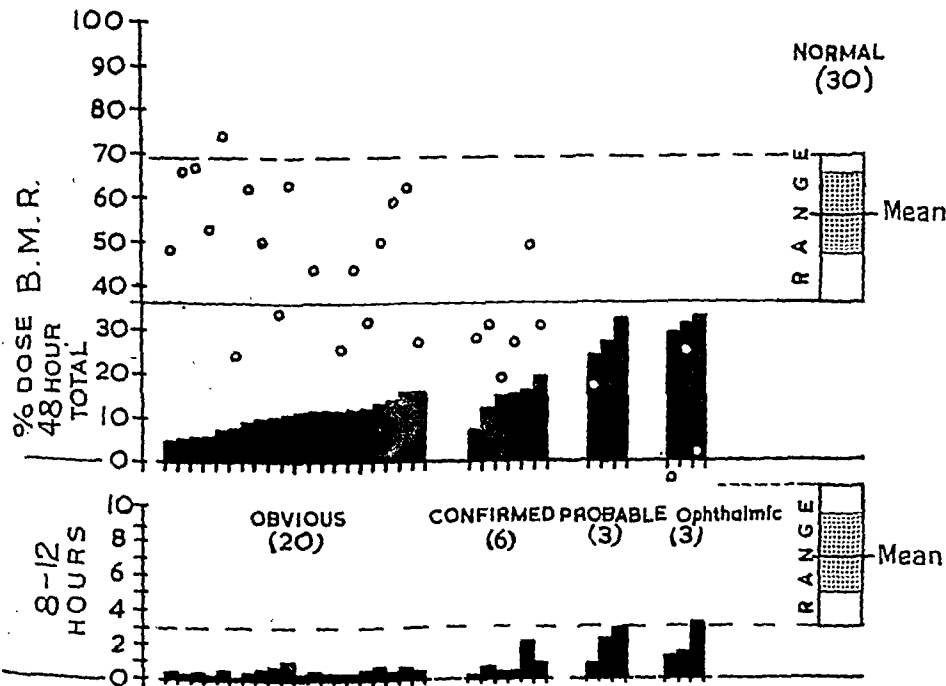


FIG. 3.—Radio-active iodine test results in both obvious and doubtful cases finally diagnosed as thyrotoxicosis or Graves' disease.

Only the forty-eight-hour and the eight-to-twelve-hour urinary excretions are shown, the normal range being indicated for comparison; dots indicate B.M.R. of cases so tested (Oral dose:  $10 \gamma$  KI +  $10 \mu$  c.  $I^{131}$ .)

on her clinical state. The second case more definitely suggests that an enlarging thyroid may be abnormally avid for iodine. It may of course be questioned whether this does not herald thyrotoxicosis. Thus we feel that none of these cases invalidates the usefulness of this test; rather they suggest that it may demonstrate thyroid overactivity too slight to be recognizable by other means.

(c) *Syndromes suggesting probable and possible hyperthyroidism.*—A series of cases in which this diagnosis was suggested but not obvious has been studied according to the following plan. On examination, each case is placed into one of four preliminary categories: (1) probable thyrotoxicosis, (2) possible thyrotoxicosis, (3) purely ophthalmic Graves' disease, and (4) probably normal thyroid function. Further examination has usually included (where possible) B.M.R., oral galactose tolerance test and a subsequent therapeutic trial with thiouracil or means appropriate to other disease. Final diagnosis is then made independently of the iodine test, as either confirmed thyrotoxicosis, probable thyrotoxicosis,

<sup>1</sup>Our subsequent observations on pregnant women suggest that pregnancy alone could not explain the low value in this case.

ophthalmic Graves' disease, and definite other disease. The presence or absence of thyroid enlargement was noted independently. The results of this test on 38 such cases of suspected thyrotoxicosis are shown in two charts. Fig. 3 includes all the cases finally diagnosed as thyrotoxicosis; fig. 4 all the cases in which this diagnosis was finally excluded; all cases with thyroid enlargement are shown as black lines. All the cases finally classed as normal thyroid function gave test results classed as normal, except for the two clinically non-toxic goitres already noted showing hyperactive iodine uptake. All those cases classed finally as

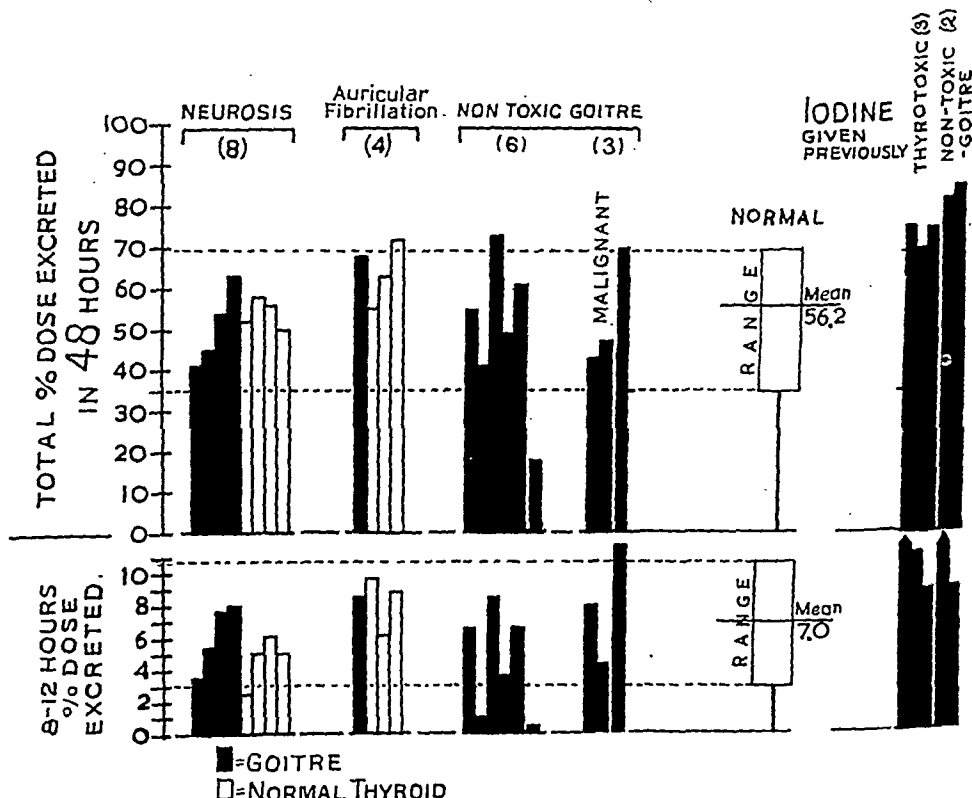


FIG. 4.—Radio-active iodine test results in cases among whom suspicions of thyrotoxicosis were not finally confirmed; as shown in fig. 3. (Oral dose: 10  $\gamma$  KI + 10  $\mu$ c.  $I^{131}$ .)

thyrotoxic gave obviously abnormal results. It will be seen in fig. 3 that there is a trend towards less abnormal iodine excretion as the diagnostic grouping becomes less certain, i.e. probably as the degree of hyperthyroidism lessens. The B.M.R. shows a similar trend.

#### SUMMARY

Urinary excretion of  $I^{131}$  has been measured in a series of cases where thyrotoxicosis was suspected clinically. The final diagnosis ascertained from the therapeutic response corresponded to the  $I^{131}$  test result in all cases in the absence of obvious renal disease with only two exceptions. These were two instances of non-toxic thyroid enlargement giving results which mimic hypothyroidism and should not be a serious limitation to the test.

#### REFERENCE

CHAPMAN, E. M., CORNER, G. W., JR., ROBINSON, D., and EVANS, R. D. (1948) *J. clin. Endocrinol.*, 8, 717.

Dr. H. Miller: Our investigations in Sheffield have been along similar lines to those described by Dr. Pochin. Table I sets out results for both thyroid uptake and urine excretion of radio-active iodine for a group of normal and toxic cases. For comparison, published figures for a group of patients in New York are also shown (Werner, *et al.*, 1948). We have here tabulated the uptake of the tracer-iodine in the gland twenty-four hours after ingestion, in order to make comparison with the New York group. We do not consider this figure in itself very reliable for diagnosis. It is to be noted that there is a fairly wide range of values obtained both for the amount of activity in the



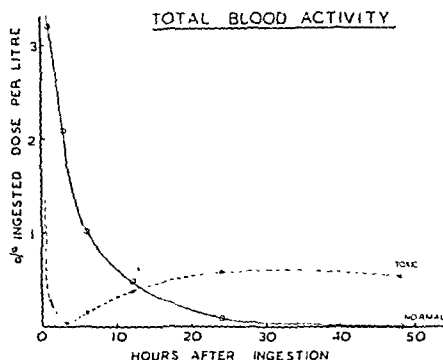
thyroid and for the amount excreted. There is also some overlapping of values for the normal and toxic groups. Figures at twenty-four hours are not apparently sufficiently reliable guides for diagnosis. There appears to be an appreciably greater uptake in normal patients in Sheffield than in those of

TABLE I.—TRACER STUDIES WITH  $I^{131}$   
SUMMARY OF DIAGNOSTIC TESTS FOR TOXIC GOITRE

| Type of case                                     | Per cent in gland at<br>twenty-four hours |         |         | Per cent excreted in<br>twenty-four hours |         |         | No. of<br>cases |
|--------------------------------------------------|-------------------------------------------|---------|---------|-------------------------------------------|---------|---------|-----------------|
|                                                  | Maximum                                   | Minimum | Average | Maximum                                   | Minimum | Average |                 |
| <i>Sheffield</i>                                 |                                           |         |         |                                           |         |         |                 |
| Patients with normal thy-<br>roid function .. .. | 54                                        | 40      | 47      | 62                                        | 21      | 42      | 10              |
| Patients with toxic goitre..                     | 82                                        | 56      | 69      | 34                                        | 4       | 12      | 15              |
| <i>New York</i>                                  |                                           |         |         |                                           |         |         |                 |
| Patients with normal thy-<br>roid function .. .. | 34                                        | 11      | 21      | 76                                        | 28      | 52      | 30              |
| Patients with toxic goitre..                     | 76                                        | 33      | 62      | 27                                        | 6       | 18      | 39              |

the New York group, and a correspondingly lower excretion rate. We believe this to be a significant observation and it may be connected with the fact that in Sheffield patients are drawn from a known iodine-starved region.

Fig. 1 shows two typical curves of total blood activity for a normal and a toxic case. A technique of counting 0.5 c.c. samples of whole blood has been used for these curves. The curves for toxic and normal patients differ markedly. In the toxic case an extremely rapid reduction of blood activity corresponding to a high clearance rate into the thyroid, is followed by a rise in activity to a



Clearance rates to thyroid at 2 hr.  
Normal 30 c.c./min.  
Toxic 530 c.c./min.

FIG. 1.

flat peak of between 0.6% and 2% of the ingested dose per litre of blood. The minimum activity occurs at four to six hours after ingestion. The magnitude of the subsidiary peak in toxic cases is related to the rate at which the thyroid secretes the active iodine into the blood-stream, this rate being determined by observing the biological half-life of the active iodine in the gland.

In the cases with no known thyroid disease there is a steady fall in blood activity after about one hour, the activity falling to one-half in about four or five hours. Such a rate of fall of activity corresponds roughly to total clearance rates from the blood of about 20 to 50 c.c. per minute, this being equally divided between thyroid and kidneys. No pronounced subsidiary peak has been observed in normal cases.

By precipitation of proteins from the plasma with trichloroacetic acid the state of the active iodine in the plasma is being investigated. It appears that after a few hours the blood activity changes from non-protein-bound to protein-bound iodine, but that later there is a reappearance of non-protein-bound activity. This is probably associated with the breakdown of organic iodine products to inorganic iodine in the tissues.

We believe useful diagnostic information is given by measurements of total activity and of protein-bound activity in the plasma.

#### REFERENCE

WERNER, S. C., QUIMBY, E. H., and SCHMIDT, C. (1948) *Radiology*, **51**, 564.

Professor E. J. Wayne: The investigations at Sheffield have been carried out in collaboration with Dr. J. F. Goodwin and Dr. H. Miller. We have attempted to assess the relative diagnostic value of thyroid uptake curves, urine excretion curves and estimations of blood activity. We have had difficulty in collecting all the urine passed during the period of observation, especially in the case of females and we do not think that studies based on urine excretion alone are always reliable. The

ophthalmic Graves' disease, and definite other disease. The presence or absence of thyroid enlargement was noted independently. The results of this test on 38 such cases of suspected thyrotoxicosis are shown in two charts. Fig. 3 includes all the cases finally diagnosed as thyrotoxicosis; fig. 4 all the cases in which this diagnosis was finally excluded; all cases with thyroid enlargement are shown as black lines. All the cases finally classed as normal thyroid function gave test results classed as normal, except for the two clinically non-toxic goitres already noted showing hyperactive iodine uptake. All those cases classed finally as

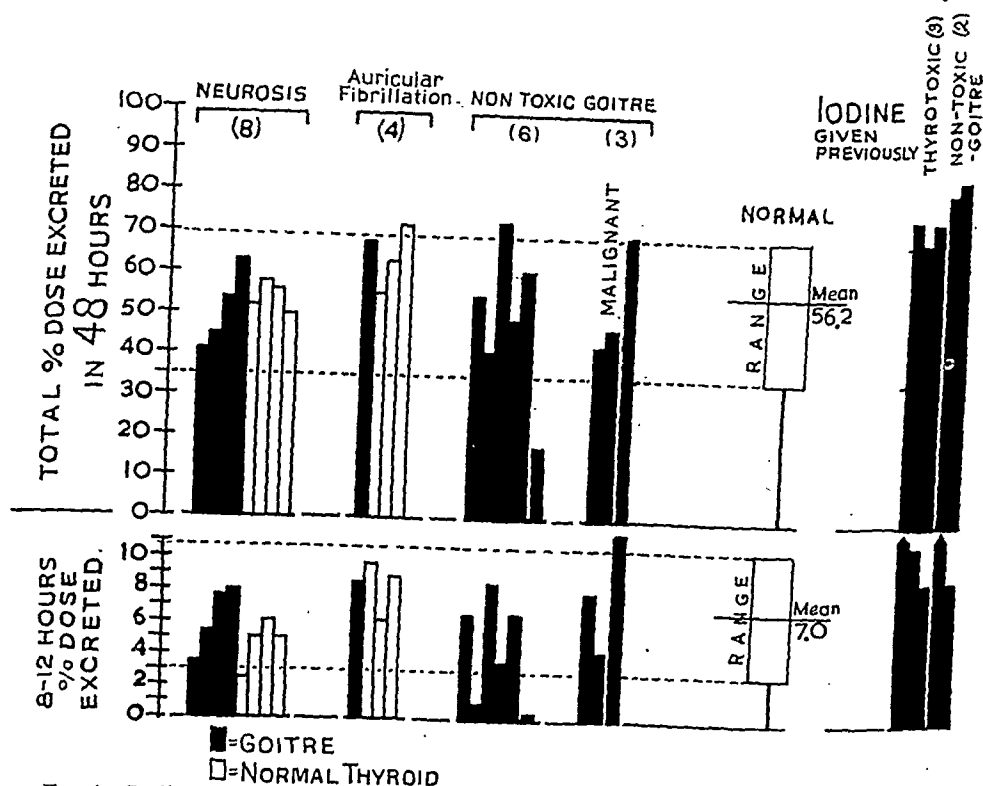


FIG. 4.—Radio-active iodine test results in cases among whom suspicions of thyrotoxicosis were not finally confirmed; as shown in fig. 3. (Oral dose:  $10 \gamma$  KI +  $10 \mu\text{c}$ .  $\text{I}^{131}$ .)

thyrotoxic gave obviously abnormal results. It will be seen in fig. 3 that there is a trend towards less abnormal iodine excretion as the diagnostic grouping becomes less certain, i.e. probably as the degree of hyperthyroidism lessens. The B.M.R. shows a similar trend.

#### SUMMARY

Urinary excretion of  $\text{I}^{131}$  has been measured in a series of cases where thyrotoxicosis was suspected clinically. The final diagnosis ascertained from the therapeutic response corresponded to the  $\text{I}^{131}$  test result in all cases in the absence of obvious renal disease with only two exceptions. These were two instances of non-toxic thyroid enlargement giving results which mimic hypothyroidism and should not be a serious limitation to the test.

#### REFERENCE

CHAPMAN, E. M., CORNER, G. W., Jr., ROBINSON, D., and EVANS, R. D. (1948) *J. clin. Endocrinol.*, 8, 717.

Dr. H. Miller: Our investigations in Sheffield have been along similar lines to those described by Dr. Pochin. Table I sets out results for both thyroid uptake and urine excretion of radio-active iodine for a group of normal and toxic cases. For comparison, published figures for a group of patients in New York are also shown (Werner, *et al.*, 1948). We have here tabulated the uptake of the tracer-iodine in the gland twenty-four hours after ingestion, in order to make comparison with the New York group. We do not consider this figure in itself very reliable for diagnosis. It is to be noted that there is a fairly wide range of values obtained both for the amount of activity in the

## United Services Section

President—Sir HENRY TIDY, K.B.E., M.A., M.D., F.R.C.P.

[June 28, 1949]

### DISCUSSION: THE PROFESSIONAL FUTURE OF MEDICAL OFFICERS OF THE FIGHTING FORCES (*Summary*)

Air Marshal P. C. Livingston introduced the subject, pointing out the various procedures for advancement which surrounded the general duties medical officer, explaining that in a mixed population of medical talent it was inevitable that some should succeed and others fall by the way.

Surgeon Commander P. G. Burgess: *The need for further post-graduate study.*—It is of special importance that every opportunity should be given to the Naval medical officer to widen his experience and make himself a better doctor, not only for the benefit of the Service whilst he is in it, but also to enable him to take his place in civilian medicine, when he retires.

There is a place for the non-specialist on the staff of hospitals in relieving specialists of some of their work thus enabling them to hold a weekly teaching round in their ward and to hold their out-patient clinic as an open session for the benefit of all medical officers in the port.

The young Surgeon Lieutenant, after a commission at sea—which is absolutely essential as it is only at sea that so many medical problems of the Navy can be appreciated—and also in a Shore Establishment, should then work for a time in a Naval hospital, not only to gain further experience but to give him a chance to show his senior officers that he has the ability and qualities for specializing.

Courses should be arranged at intervals of five to six years, not in a Naval hospital but in a civilian hospital where the medical officer would come in contact again with the diseases of men, women and children of all ages.

Major A. D. Young: General duties medical officers may be described as :

(1) A small minority who, by virtue of their knowledge of medical tactics, administration and operational planning, will rightly attain high rank in war.

(2) The majority who are unlikely to reach the rank of colonel and who will not be promoted beyond this rank.

*The ambition and ability of the individual officer.*—It is considered that the officer whose ambition is to become the D.M.S. of an Army Group will, *ipso facto*, pursue military rather than professional knowledge. His ability can be determined by his superiors and, where suitable, he can be earmarked as a likely future general officer. The early selection of such officers is important and it is interesting to note what Field Marshal Sir William Slim has written on the subject of "Higher Training for Combined Command" (*J. Roy. Unit. Serv. Inst.*, 1947, 92, 507.)

*Conclusions.*—It is important to realize that all general duties medical officers require medical training.

The outstanding officer, who is regarded as likely to reach general rank, requires special training in military medicine, hygiene (including the physiological and pathological aspects of the effects of service in arctic and tropical climates), and surgery, aviation medicine, and the medical aspects of atomic and bacteriological warfare. This would mean courses and refresher courses but would not entail his employment as a medical officer in charge of troops after his first six years' service. The majority of general duties medical officers would require to hold at least as many purely professional appointments as administrative ones. This would undoubtedly mean that many Regular specialist officers should have certain junior administrative appointments every now and again instead of having specialist appointments during most of their service, and also that more civilian specialists would have to be appointed to emergency commissions. Finally, it is emphasized that there are three main

most valuable single figure in our experience is the plasma clearance rate at two hours, but a complete study including observations on the shape of the build-up curve gives additional valuable information and is advisable in the present state of knowledge of thyroid function.

In studying the activity of blood we have found technical difficulties in separating the thyroxine, diiodotyrosine and inorganic iodine fractions by the butyl alcohol method of Taurag and Chaikoff (*J. Biol. Chem.* (1948) 176, 639). The separation into protein-bound and non-protein-bound fractions by precipitation with trichloroacetic acid is much simpler and since there is evidence that diiodotyrosine is rapidly broken down in plasma to form inorganic iodide (Leblond and Sue, *Amer. J. Physiol.* (1941), 134, 549), it gives much the same information as the butyl alcohol separation.

Dr. Max Reiss: In the human we have found that thyrotrophic hormone increases the avidity of the thyroid for  $I^{131}$  and decreases the excretion rate. The different reactions of hypothyrotic patients to treatment with thyrotrophic hormone can be used for differentiation between primary (thyrogenous) and secondary (hypopituitary or cerebral) hypothyrotic cases.

Mr. J. E. Piercy (discussing Dr. Pochin's paper): Radio-active iodine can be valuable as a guide to the surgeon in addition to its other uses. In cases of clinically apparent carcinoma of the thyroid, when both lobes are involved, it is desirable to remove all of the gland with the exception of a posterior strip on the less affected side—this being often difficult to decide—in order to ensure the safety of at least one recurrent laryngeal nerve.

At the New End Thyroid Clinic we recently gave a tracer dose of radio-active iodine to a patient with clinically apparent carcinoma of the thyroid. Dr. Pochin then ascertained by means of the Geiger Müller counter that although very little radio-active iodine was taken up by the gland, the left lobe contained five times as great a concentration as that of the right. The major part of the remaining normal thyroid tissue, therefore, was present on the left side.

At operation I removed all of the gland with the exception of a posterior strip on the left side. Dr. Pochin subsequently found by means of autoradiographs that the excised thyroid mass showed no uptake of radio-iodine. Faint areas of uptake were demonstrated locally, however, which corresponded to the incompletely destroyed thyroid tissue still remaining in the left side of the neck.

Information gained by means of the Geiger counter, therefore, enables us to remove without question the lobe which is most involved by growth and to leave behind the posterior margin of the, less affected side.

Dr. George Ansell (Department of Medicine, Liverpool University): Working in collaboration with Dr. J. Rotblat of the Department of Physics, we first used  $I^{131}$  for the diagnosis of intrathoracic goitre in 1947 (G. Ansell and J. Rotblat (1948) *Brit. J. Radiol.*, 21, 552-558) and have now examined 9 suspected cases. An intrathoracic goitre was demonstrated in 4 patients and the diagnosis was subsequently confirmed. In 2 others the mediastinal tumours failed to take up  $I^{131}$  and later it was shown that these were not goitres. Two patients were suspected of having "deep" goitres. These were not operated on but the radio-active iodine results agreed with the clinical and radiological findings. Results in the remaining case were vitiated by the patient taking a cough mixture containing iodides.

Dr. A. W. Spence: I was interested in Dr. Doniach's "rings and blobs". In the preparation of the sections inorganic iodine is washed out and hence the radio-active iodine demonstrated is organically bound. According to Leblond radio-active iodine is found in the colloid soon after injection, that is, when most of the radio-activity of the gland is in the diiodotyrosine fraction and little in the thyroxine fraction. He has suggested that the formation of thyroxine from diiodotyrosine may to a large extent take place inside the colloid. I should be interested to learn whether there is agreement concerning this hypothesis.

The material presented at the Afternoon Session will be abstracted in the *Journal of Endocrinology*. The programme was as follows:

#### FILM

Transplantation of the Pituitary Gland in Humans.—By Professor KUBANYI (Budapest) (shown by Dr. RAYMOND GREENE and the PRESIDENT).

#### PAPERS

Synthetic Thyroxine in the Treatment of Myxœdema.—Dr. F. D. HART and Dr. N. F. MACLAGAN.

Further Observations on the Use of Urinary Pregnanediol Assay as a Pregnancy Diagnosis Test.—Dr. G. I. M. SWYER.

The Excretion of Œstrogens during Labour.—Dr. BARBARA E. CLAYTON and Dr. G. F. MARRIAN.

Effect of Œstrogens on Menstruation Rhythm.—Dr. A. N. RICHARDS and Dr. P. M. F. BISHOP.

Clinical Syndrome Associated with Kimmelstiel-Wilson Lesions of the Kidney in Diabetes.—Dr. I. GILLILAND.

Diagnostic Tests in Diabetes Insipidus.—Dr. A. G. G. LEWIS and Dr. P. M. F. BISHOP.

Œstrogens and Citric Acid Excretion.—Dr. MARION S. EDWARDS and Dr. MARY E. WOOD.

Paget's Disease with Signs of Hyperparathyroidism: A Case Report.—Dr. K. O. RAWLINGS and Dr. P. M. F. BISHOP.

often interested in other cases he sees when visiting. Clinical meetings when held should be widely circulated to ensure that all R.M.O.s are cognizant of date and time.

Above all, from a professional point of view, he must be pursued with problems and asked to submit views and recommendations on current equipment or procedures.

From a unit point of view the R.M.O. is invaluable as a liaison officer.

On completion of three years as R.M.O., and, if he has decided to apply for a permanent commission, it is suggested that he is sent for a short course at the depot prior to being selected to train junior officers at the depot or commence staff training. Depending on his success as an R.M.O. he may be considered for selective promotion, and an appointment for one year as a Staff captain medical in a Command or G.H.Q. would give him sufficient experience to be appointed as a D.A.D.M.S. of a District/Division or equivalent formation. After two years in this type of appointment it is felt that Staff College is the next step and War Office Selection would probably occur at this stage of his service.

**Squadron Leader J. B. Loudon :** The majority of newly qualified medical practitioners are not in sympathy with the Armed Services partly on account of their training, and partly because they share a traditional British dislike for the Services as a career.

If it is considered desirable, both from the point of view of the Services and that of the newly qualified doctor, that he should not be a conscript, plans should be made to increase the status of Service Medicine in the eyes of the profession and to improve the facilities for post-graduate study in inter-Service hospitals. Applicants for short service and permanent commissions would not then be lacking.

Meanwhile the opportunities for clinical meetings for all Service medical officers should be officially encouraged to take place in Service establishments.

**Surgeon Commander T. G. B. Crawford :** The medical services need administrators and specialists. For both equally, early selection and prolonged training are required, or quality will suffer.

Specialists can always be obtained from civil sources in emergency. Administrators of the medical services are in a speciality of their own. They should fill the higher ranks in the interests of efficiency and of all medical officers. Their natural source is the general duties officer. It is essential that their professional knowledge and sympathy should be maintained.

The real problem is the future of senior specialists, who have been educated as technicians. Something in the nature of a Corps of Specialists may be the solution.

At the age of 35, every medical officer should have a clear idea of his future prospects in the Service, and be professionally and financially competent to transfer to the National Health Service.

If the medical services are to be efficient in war, they cannot be run parsimoniously in peace, with regard to either money or doctors. The training of administrators is just as necessary to the medical services as the training of Admirals, Generals, and Air Marshals is to the Fighting Services.

**Major A. Bennett :** What courses are open to the young doctor after qualification and after completion of his junior hospital appointments?

(1) An appointment in the National Health Service. (a) In a junior hospital post with a view to specializing. (b) As a general practitioner, probably as an assistant in an established practice. This is assuming that he is not required for National Service in the armed forces. (2) Call up for National Service for the specified period in the medical branch of one of the Fighting Services, after which he will proceed to course (1). (3) During course (2) he may elect to apply for a short Service commission, with or without a view to a permanent Regular commission.

The above three courses cover the majority of medical men, and other branches of medicine such as the Colonial Medical Service, or Public Health, &c., will not be considered here.

The doctor who joins one of the Fighting Services, for instance the Royal Army Medical Corps, will find that on completing his three weeks at the R.A.M.C. depot and Military School of Hygiene, where he is taught the elements of Service life, he receives a posting to a medical appointment.

This is usually either (a) to a general hospital ; (b) to a camp reception station ; or (c) the charge of a medical inspection room.

The medical branches of the Fighting Services can now be fairly compared with State Health Service, and the prospects of officers will be seen to be extremely favourable in such a comparison.

The question of combining the Civil and Fighting Medical Services should be explored, with a skeleton administration staff for the organization of foreign service, and for the expansion of the fighting branch in time of war.

types of medical officers in the Services—the outstanding administrative officer, the average general duties medical officer and the specialist. All are essential to the efficient running of the Service and the more they know of each other's problems the more efficient the Service will be.

**Group Captain F. E. Lipscomb:** Every medical officer should be a general duties medical officer for the first two to three years of service. This would be to the advantage of the Service and the individual.

Specialization should be available to a very large proportion of medical officers between the third and sixth years of their service. Those not selected should be informed at once so that they may know the limit of their prospects.

Medical administration should be recognized as a full and most important speciality following adequate training. This would provide a career for a considerable number of medical officers and would be of great benefit to the Services.

It is impossible in any organized military medical service to provide a full career in clinical medicine without specialization. Such specialization is limited by the requirements of the Service.

**Surgeon Lieutenant-Commander L. D. Arden:** Comment on future prospects for the average serving medical officer is based upon experience in His Majesty's Ships at home and abroad, in Royal Naval Establishments ashore, such as barracks and hospitals, and service with Royal Marine units working with the Army.

There is an obvious disparity between the conditions for general duties and specialist medical officers in the Fighting Services, and an even greater gap between the previously mentioned groups and the practitioners in the National Health Service.

Accelerated promotion, for distinguished service or conspicuous professional merit, is rarely, if ever, awarded in the Royal Navy.

Promotion to higher rank by special selection increases the spirit of competition and encourages efforts to improve knowledge and skill, which should undoubtedly have their reward.

This idea of payment for results might well suggest that an officer could specialize in administration just as an officer specializes in bacteriology and be granted an equivalent status and remuneration.

It is thought advisable that all medical officers should be granted greater opportunities for professional advancement, such as post-graduate study and the chance to work for higher qualifications.

As a general duties medical officer of some ten years' standing, I have found that the only security for length of tenure in an appointment is when on service afloat, periods when there is little opportunity for clinical work.

Further attention might be given to the recent change for the worse in zones for promotion in the Navy.

**Major J. C. Babbage:** Let us define the general duties officer as the General Practitioner of the Fighting Services, relatively young, in the same way as his clientele are of younger age-groups. A "Jack-of-all-Trades, Master of None," it may be said in his more junior days, but never let us minimize the invaluable experience he accumulates over a wide range of medical subjects.

We next ask ourselves "Wherein might he acquire this experience? What type of training should be evolved to fit this officer for his duties?" In the R.A.M.C. the pre-war Depot training coupled with the course in Tropical Medicine, Hygiene and Entomology, of a duration of approximately three months was excellent.

A further month's training should now follow in regimental duties with a unit as the regimental medical officer. This will decide whether he wishes to continue as a regimental medical officer or prefers general duties in a hospital. It is accepted that the later success and experience of a G.D.O. comes from arduous but happy times spent with a unit either in action or not. Thus for junior medical officers when on duty as R.M.O.s there should be a definite tenure of appointment for three years. Where the unit goes, so the R.M.O. patiently follows. The postings should be War Office controlled but limited to the major units of the current Order of Battle.

With the unit his broad training must be pursued. Because he is the only medical officer in the unit, he should not be precluded from attending an administration course for regimental officers or an M.T. course—both very valuable if he later joins a field medical unit. It is incumbent on the unit to recognize that they are responsible for this general training of their medical officer. Paratraining or air support training should be actively pursued.

If the unit is in the vicinity of a Service hospital there should be hospital rounds for R.M.O.s and G.D.O.s arranged by the specialists on interesting cases which have been admitted. The R.M.O. usually, unless distance prevents him, follows up his cases but is

(2) The G.D.O. should be able to investigate his own cases and present them to a specialist himself; he should officially participate in the running of his parent hospital.

(3) The ritual of routine examinations and inspections which has to be performed by the G.D.M.O. must be reduced.

(4) Finally, a comprehensive medical course (possibly leading to full specialization) should be undertaken after only five years of general duties.

**Squadron Leader W. J. Lloyd Harries:** *The young Service doctor—his problems.*—The medical officer has difficulty in forming an idea of the plan of his Service life, as he constantly jumps from one Air Ministry Order to another, gleaning information here and there in trying to piece together a complete picture. If he decides to dedicate his career to the Service, and goes into one branch of medicine, say, anaesthetics, is he likely to be left behind in the race for promotion by his friend who stays in the administrative side, because on the administrative side there is more room for promotion as compared with the anaesthetics' side where promotion is very limited?

Again, should he be passed over in the race for promotion, is he at liberty to retire voluntarily after he reaches the pensionable age in the rank attained or are obstacles placed in his way?

There seems to be a considerable delay—many years—in granting study leave, this I presume to be because little or no study leave was granted during wartime and that now study leave is being granted in rotation.

Again, can study leave be granted for as long as two years? This period appears to be the minimum amount of time spent in a resident appointment, at a recognized hospital, before the Royal College of Obstetricians and Gynaecologists will allow a candidate to sit for the M.R.C.O.G.

The Service hospitals are few in number and lack the clinical material seen in civilian hospitals which contain patients of all age-groups.

**Surgeon Captain R. W. Mussen:** *Naval Doctoring as a speciality or profession in itself.*—I have always looked upon Naval Doctoring, or Marine Medicine, as a speciality in itself. For a long time we have had our specialists in the purely professional subjects such as medicine, surgery and others. They have been individuals who have had special training or qualifications in their particular subjects, but nevertheless they are liable at any time to be appointed to general duties.

During the war, further individual specialization occurred through the tremendous increase of mechanized warfare. Led by the Royal Air Force, with the perception of personnel medicine, we had our medical physiologists and other experts of this kind. This was carried still further with the development of the possibilities of atomic and bacteriological warfare. There has unquestionably been some antagonism, or possibly a lack of understanding between the professional types and the so-called scientists who thought that some of their activities were outside the field of medicine proper. I do not think that this is correct and feel that doctors must keep up with all matters which may concern the health, efficiency and welfare of the people for whom they are responsible. They must at times get away from the narrow technicalities of specialized surgery and medicine. Another way of looking at this is that if the doctors do not interest themselves in these matters, someone else will, and we will find ourselves ousted from matters in which we should be concerned.

The term, general duties officers, in the case of the Navy, includes many medical officers serving in ships, barracks, dockyards and other places. Incidentally, a large number of these are already specialized, and doing a period of general duties in between specialist appointment, and others could be called specialists in Aviation Medicine or Industrial Hygiene. The general duties officer, or as I would prefer to call him, the Naval doctor, is interested in everything which concerns the health, efficiency and welfare of his men. Under certain conditions in the tropics, on long cruises and under other particular conditions, one may find a falling off in efficiency, drop in morale or other circumstances in which the well-trained Naval doctor can help. At the same time, his role is that of field observer of conditions of men in the Fleet or Shore Stations. By the nature of his appointment he has unique opportunities for observing reactions of men to their environment in all types of ships, in all climates, and under active service conditions.

The one condition is that on entry, he should receive suitable instructions in the speciality of Naval or Marine medicine, about which the average newly qualified officer knows little or nothing. A well-balanced course of about six months in duration should cover many and diverse subjects.

Here we have the basis for instruction in the speciality of Naval Medicine. If this should be followed by a commission at sea, the medical officer may describe himself by that old and honourable title—"A Naval Doctor".

The interest of the G.D.M.O. in clinical work must be fostered, particularly the newly joined man, who comes straight from civil hospital work, where he has been imbued with a spirit of enthusiasm for his professional work, and a terrific appetite for work in the practice of the profession which he has chosen for his career.

It is suggested that before leaving the depot, every newly joined officer should be interviewed by an "appointments" officer, who should ascertain the branch of Service Medicine in which he is interested, and that on leaving the depot the officer should be posted straight to a suitable appointment, such posting to be of a permanent nature as far as possible. He should not be posted to a command pool, to be employed in any vacancy that may arise.

**Group Captain A. Dickson :** The general duties medical officer employed on a Station or Unit is the first line of defence against loss of man-power from preventable medical causes and as such he must be adequately prepared and equipped for that onerous duty. If he is to be successful in his efforts it is essential that he should be encouraged and assisted to keep himself at the highest peak of efficiency.

What does this imply?

Firstly : He must be contented with his lot.

Secondly : He must be given the opportunity to keep abreast of all developments and advances in such branches of medicine as affect his role—and that excludes very little.

Thirdly : He must see a career in his own branch of Service Medicine at least equal to that of his colleague who has chosen another path.

The third point requires a regular ladder of ascent on a parallel with the specialist in other subjects. He should pass from Medical Officer on a Station to Senior Medical Officer on Stations of different sizes and types, administrative employment in large Medical Units, and staff appointments of various grades. The principle of accelerated and selected promotion for ability should be in evidence.

**Surgeon Lieutenant-Commander J. Glass :** *A brief outline of training for the first fifteen years of service of a General Duties Naval Medical Officer.*

*First course.*—On entry—Short Service Commission. Duration three months. Examination on completion.

This course should be similar to the prevailing course at the Royal Naval Medical School, with an emphasis on: Naval medical organization ashore and afloat. Naval history. Physiological problems. Chemical, biological and atomic warfare problems. Public health problems. Medical statistics and records. Naval medical history. X-ray procedures. Tropical medicine.

*Second course.*—After five to eight years' service. Duration nine to twelve months. For candidates selected for the permanent medical service. Examination on completion.

This course should consist of an intensive study of: Medicine. Surgery. Public Health. Medical statistics. Physiology. Naval architecture. X-ray procedure. Administration, and medical problems in relation to : Aviation, diving, submarines, amphibious operations, chemical, biological and atomic warfare, and tropical medicine.

A paper or thesis should be submitted at the end of this course. From this group certain selected candidates should be chosen and given the opportunity of pursuing a higher qualification at civilian institutions.

*Third course.*—After eight to twelve years' service. Duration six months. For qualification to Surgeon Commander's rank. Examination on completion.

This course should be similar to the second course, with, however, the emphasis placed on administration of the special departments of Medicine, Surgery and Public Health.

From this group selected medical officers should be seconded to the Army, Air Force, or a Foreign Navy, for six months to establish a firm liaison with the other Services. A report of the tour of duty should be submitted.

*Fourth course.*—After twelve to fifteen years. Duration six months.

This course should consist of modern developments study groups in any three optional subjects of Course 2.

A paper or thesis to be submitted on completion of course.

**Captain B. J. Sproule :** The advent of the National Health Service has levelled the conditions of work between the Services and civilian practice and the main attraction to the Services in the future lies in the professional opportunities that are available.

The following recommendations are made:

(1) The "Graded" Specialist should be abolished in order to raise the professional outlook of the G.D.O., who should be able to attend short courses to improve his working knowledge of the diseases most commonly encountered in the Services.



**Group Captain R. H. Stanbridge:** The following suggestions are based on the idea that an interest in aviation and aviation medicine should be encouraged more than is done at present.

*Amedates*—For members of Hospital O.T.C., Gliding or Flying Clubs.

*Opportunities to learn to fly*—More to be trained as pilots, thus leading to accelerated promotion to Squadron Leader on qualification as pilot, and on completion of a special course in aviation medicine. This should be built up at Farnborough—say a two to three months' course, on similar lines to the School of Aviation Medicine in America.

*Flying personnel medical officers*—He would then become what is now known as a Flying Personnel Medical Officer, although the present system would require changing as follows: The appointment to be made earlier, i.e. as a Junior Squadron Leader; it should be limited to two years; and followed by an appointment to one of the following special administrative posts (F.P.M.Os. to-day tend to go on year after year with no definite future. By shortening the period an increased total number could be employed and the appointment could be followed by a special administrative post).

*Special administrative posts with Squadron Leader rank:*

(a) *D.S.M.O. of groups:* These would be in place of and carry out the duties of present Pool medical officers, so giving experience of administration, as well as of different types of stations, and would increase the knowledge of its units by groups;

(b) *S.M.O. of stations:* Acting rank to be given where established;

(c) *Appointments at hospitals and medical units.*

(d) *Increased establishment of teaching staff at Farnborough:* A fuller Aviation Medicine Course to be instituted.

*Special administrative posts with Wing Commander rank:*

(a) Each hospital to be established with Wing Commander second in Command. This gives valuable and interesting administrative experience, and by combining the duties of President of Medical Boards and Officer i/c Training should increase the efficiency of hospital administration and at the same time relieve the specialist of what he usually considers to be an uncongenial task.

(b) The appointment of D.P.M.O. Hygiene at each Command to be reserved for him as the work links up logically with his post. The care and well-being of flying personnel and of those factors tending to produce fatigue in air and ground crews are his province. His administrative posts will have prepared the way on that side and he would be more useful to a P.M.O. and A.O.C. than a D.P.H. who had little contact with unit life.

In the past this post has been linked with the possession of a D.P.H. although it has been as efficiently held by general duties medical officers (as a specialist post it is probably unique in this respect). In fact, if the above suggestions of increasing establishments are met by that invariable response "we have not got the bodies to do it", one answer is that study leave for the D.P.H. should be strictly limited and the places so freed (about half) could go to general duties medical officers who could learn to fly or do a special course in aviation medicine. (In any event most of the ground of the D.P.H. is covered by the D.I.H. or D.T.M. and H.) Incidentally, unit hygiene and sanitation which is regarded with so much suspicion by young medical officers, may have more interest when linked with the prospect of becoming fairly rapidly a Wing Commander D.P.M.O.(H.).

*Staff College.*—At least half the vacancies to be reserved for him.

*Special posts in Group Captain rank:*

These follow logically, i.e. the C.O. of hospitals; C.O. of Training Establishments; P.M.O. of Commands.

*On Retirement.*—Certain posts to be earmarked, e.g. civil aviation and Government appointments.

**Surgeon Commander S. Miles:** *Is medicine in the Service a career?*—This short paper is primarily a plea for as little change as possible in the present scheme of medical service in the Navy, for the encouragement of personal enthusiasm for the Service and the profession, and the minimization of standardized direction.

(1) We join because of three main factors:

*Glamour:* The more honest amongst us will admit that they were attracted to the Navy (or other Services) by the colourfulness of its traditions and practices, by the social opportunities it offers and by the inherent British kinship with the sea, in fact, to hold the King's Commission and travel proudly.

*Pay and Prospects:* For the impecunious young doctor, rather tired from excessive study and as yet unburdened by family commitments, the apparent easing down of mental exertion with, even now, fairly good pay and prospects of specialization and promotion is a great draw.

Major E. A. Smyth: The general duties medical officer in the Services should be a well-trained general medical practitioner, capable of undertaking the common types of emergency surgery and certain carefully selected types of "cold" surgery.

His professional work must include a knowledge of (1) Curative medicine, (2) preventive medicine, (3) general knowledge of Service conditions. The following training is suggested:

(a) About four years' trainee apprenticeship in the different departments of the Service hospital. In some specialities, venereal, skin diseases, &c., a period of a couple of months would be sufficient. In other specialities such as general medicine and surgery, a period of twelve to eighteen months would be essential.

(b) At least six months' practical apprenticeship in preventive medicine establishments abroad.

(c) Short courses at a Service Medical College and a Service Staff College.

Group Captain H. C. S. Pimblett: *Professional contentment.*

(1) *Relations with other Fighting Forces.*—The Royal Air Force considers the medical officer in its own uniform as essential in maintaining its high operational morale and undoubtedly the medical officer in the last war played a tremendous part in maintaining the fighting efficiency of our pilots. Nevertheless, from personal experience of close active service co-operation with the Army, it seemed obvious that in certain areas there was a considerable overlapping of staffs. It would seem rather unnecessary to have three or more medical officers sitting down, not infrequently in the same building, administering the hygiene of both Army and Air Force Units operating in the same areas, and it should surely be possible on occasions to economize medical man-power by combining the services of certain members of both Army and Air Force medical staff. After all, there is not much difference between certain aspects of military medicine in, for example, the Royal Air Force and the Army, and it is suggested that in peacetime a certain number of general duties medical officers, preferably holding staff appointment, could be interchanged for periods of, say, a year, and thus become acquainted with the difference of routine—which is probably only slight in each of the Services. Not only would the professional outlook of the regular officer be stimulated, but he would develop a greater appreciation of the work and problems of his sister Services and certainly this would go a long way to dispel any inter-Service professional jealousy which may exist at the present time.

(2) *Medical officers who fly.*—The Royal Air Force has long encouraged their medical officers to become pilots, and the prospect of flying has attracted many most suitable medical men into the Service. It should be said that the greatest encouragement to train medical officers as pilots has been from members of the general duties branch itself (especially from officers of and below the rank of Wing Commander) and why? The answer is complex but it is certain that the operational pilot, especially if he is young, appreciates the practical interest of the medical officer in his problems, both psychological and physiological, connected with practical flying. A few specially selected medical officers are at the present time being given a full flying training course: their number is limited and they are regarded as members of a closed circle by other medical officers. Before the war many medical officers were taught to fly on elementary land planes sufficiently well to fly light aircraft—and this without interference with their Station medical obligations. It is by no means essential that every medical officer who wishes to fly should take the more advanced course: if many more younger medical officers were allowed to fly there would be more keenness to join the Royal Air Force as a Regular officer.

(3) *Opportunities of retirement.*—The majority of Regular medical officers now serving were informed before joining that they would be given antedates for hospital appointments held in civilian life in order, of course, to improve the professional status of the Service. They were also informed (but, of course, not guaranteed) that they would be able to retire on pension or gratuity at minimum retiring ages and were told their compulsory retiring ages. This has now been swept aside, the retiring ages have been raised. The medical officer has lost the pensionable rights of antedate given to him on joining the Service and he considers that there is considerable difficulty in voluntarily leaving the Service at his minimum retiring age. The officer was given the right to continue with the old conditions but, on promotion, he automatically lost this privilege; this is unfair. Why should a man serve longer than he had bargained for? Let the grumblers be free to retire when they like—very few would actually go and there would be far less grumbling.

(4) *Post-graduate study leave.*—The Service has, rightly, almost insisted that regular medical officers obtain higher qualifications. Additional study leave should be generously available for those officers of the rank of Group Captain and above prior to their retirement from the Service.

Squadron Leader H. N. H. Genese: Three ways in which the future of the general duties officer might be better assured are:

- (a) By according the medical administrator a status equal to that of a clinical specialist.
- (b) By improving the general duties medical officer's opportunities for clinical specialization.
- (c) By improving the general duties medical officer's opportunities for routine medical practice.

Surgeon Lieutenant-Commander P. H. K. Gray: On joining the Royal Navy some twelve years ago I had, from a newly qualified doctor's point of view, a varied career ahead of me. Travel, a chance of studying tropical diseases, the possibilities of a bright social future and participation in practically any line of sporting activity one might desire. These opportunities were not, in my opinion, so readily available to my civilian colleague.

There is to-day a marked tendency to specialize. The general duties officer, who is the backbone of the branch, will, however, persist, and it should be his aim to become a first-rate doctor as well as a first-rate officer.

Every general duties officer should have a course in administration.

There should be closer co-operation between the general duties officer and his civilian counterpart.

Every general duties officer should do spells in one of the bigger hospitals.

The promotion course should be re-instituted. Short post-graduate courses of, say, a month in general surgery and medicine are, in my opinion, of doubtful value.

Unless he wishes to take up some other subject, he must endeavour to become an expert in Naval and Military hygiene and administration, though this should not be at the expense of his knowledge of classical medicine.

Surgeon Lieutenant G. Pollitt: The medical officer in the Services has very often to be his own clinical pathologist and specialist, because units of the Fighting Services are often stationed many miles from the nearest town, or are in ships at sea. Also in Service Medicine, medical officers often spend a considerable amount of time attached to small ships or units where the clinical material is slight.

Post-graduate courses should be particularly designed as refreshers in general medicine as applied to service age-groups, with a short course in clinical pathology, with special reference to microscopy.

In the Services the great majority of medical officers are attached to units, some large, some small, but all containing a large percentage of theoretically healthy individuals. The result is that the clinical material, as already mentioned, is slight. Acute cases are usually discharged to hospital, often some miles away, with the result that it is difficult for the unit medical officer to follow up his cases. The obvious answer to this is that all medical officers should do a spell in hospital every few years. However, Service hospitals must carry their specialists, as in the case of civilian hospitals. Medical officers with higher qualifications are the obvious choice for the specialist appointments, and officers with higher qualifications are therefore going to keep the hospital jobs permanently filled, with the exception of a few junior appointments, or else they are going to spend a considerable time attached to small units with little outlet for their accomplishments.

Wing Commander G. Gilchrist: The doctor who elects to make the general duties branch of one of the Services his permanent career will find that he is dealing, in the main, with a body of fit young adults, and that the work is, in fact, mostly preventive medicine. Secondly, as he progresses up the tree of promotion, his work will steadily become more administrative, and less clinical. But, and this is important, although he is becoming an administrator, he is still dealing in preventive medicine, and is now responsible for a far wider field than when he was a practitioner. He is, in fact, becoming a specialist of preventive medicine, in his own right and within his own general duties branch.

At this point, the budding young general duties specialist must have available the same opportunities to improve his knowledge and worldly position as are available to his colleagues of the specialist branches. He must know that if his record is good, he has a reasonable chance of study leave for the purpose of taking higher qualifications in the field of preventive medicine, for example, the D.P.H. or the D.T.M. & H., or there must be available to him senior courses in administration and staff duties. The obtaining of a diploma, or of a good pass mark on a course, must carry with it the prospect of financial advancement in the form of a gratuity or antedate in promotion. The antedate should also be much more freely used than is the practice to-day, and should be awarded to men with a steady record of reliable and meritorious service. An excellent time for a review of possible antedates would be at

*War Service:* For those who regard war as inevitable, a Service career gives promise of the minimal disorganization of one's life with its advent.

(2) Once we are in we either:

(a) Hate it and get out.

(b) Enjoy the Service life with medicine almost an incidental subsidiary. We become firstly Naval officers. Some become hard-drinking, hard-playing, immensely popular individuals and often very successful ships' (or regimental) doctors.

(c) Remain faithful to medicine primarily, resent the just interest of our lay superiors in our work and kick against the necessary restriction of discipline and wider demands of the Service. We clamour for repeated hospital jobs, courses, and should we be lucky enough to become specialists, we sink gratefully into a deeper groove of hospital practice, hiding our gold braid under a white coat, or

(d) Achieve the happy ideal where our Service and Medical work is united, wherein, whether we become specialists or remain "salt horses", our interest is "Service Medicine" first and foremost.

(3) Sooner or later: Having served in various ships and establishments we are conscious in our professional experience of a liking for, a leaning towards, and an increased ability in one, above all, of the many specialties, be it general medical administration, general Service practice, air medicine or one of the purer medical or surgical branches. If we are worthy, the opportunity to develop our talents exists and our career develops in its fullness to the advantage of the Service.

The following points, admittedly open to wide discussion, are submitted :-

(i) A Service doctor, whatever his ultimate aim, should serve an apprenticeship at sea or in the field, doing general duties for at least two years.

(ii) His interest in medicine should be kept alive after the above two years by frequent appointments for general duties in Service hospitals or sick quarters.

(iii) Opportunities and encouragement should be given for those whose medical practice is necessarily limited to take postal courses in chosen subjects, take part in the activities of local medical societies and organizations outside the Service.

(iv) Specialization should *rarely* come until there has been ten years of unreserved experience in all the ramifications of Service medicine. When specialization is reached the development should continue and increase with maturity and promotion, and not be swamped by the obligations of administration.

(v) "Medical Administration" should belong to a special subject of equal status with others.

(vi) Some form of working agreement with the National Health Service should be established whereby, should opportunity arise, Service families and spare-time patients may be accepted and treated.

**Wing Commander S. R. C. Nelson:** *Administration as a Service Speciality.*—In due course general duties medical officers reach posts where they must assume administrative responsibilities, and as they become more senior, those of them who have the ability become relatively of greater value to the Service. It is entirely possible to imagine such a medical service without any given type of specialists but it is impossible to imagine an efficient medical service without adequate administrative control. It is therefore considered that officers who show ability in administration should be given special training by the Service. Having received it, they should receive recognition, such as accelerated promotion exactly parallel to that given to specialists in clinical subjects. It might be thought that this is advocating making every Service medical officer a specialist; such is not the case. It is considered that a Service requires a maximum of 10% of all officers, qualified as administrative specialists, and who would have a rate of advance to the rank of Group Captain equal to that of clinical specialists. In higher ranks this is in effect what happens to-day as promotion is by selection. The non-specialist medical officer would therefore never reach Air rank, but it must be remembered that this situation is not peculiar to the Service. It is exactly paralleled in civil life where the majority of doctors earn a fair competence but never advance beyond that. In either Service or civil life advance is based on experience and ability.

The G.D. medical officer who reaches Air rank does so because of his administrative ability. He, who, until this point, has been at a disadvantage because he has not had accelerated promotion and the pay that goes with it, thus reaches parity with his specialist colleague. It is therefore submitted that officers with special aptitude and training in medical administration should be considered to be specialists and should receive accelerated promotion or any other benefits on the same basis as do the clinical specialists. This would place these two types of officers who are of equal value to the medical service on a par during the important middle years of their careers. It is considered only just that they should be on an equal footing.

**Squadron Leader H. N. H. Genese:** Three ways in which the future of the general duties officer might be better assured are:

- (a) By according the medical administrator a status equal to that of a clinical specialist.
- (b) By improving the general duties medical officer's opportunities for clinical specialization.
- (c) By improving the general duties medical officer's opportunities for routine medical practice.

**Surgeon Lieutenant-Commander P. H. K. Gray:** On joining the Royal Navy some twelve years ago I had, from a newly qualified doctor's point of view, a varied career ahead of me. Travel, a chance of studying tropical diseases, the possibilities of a bright social future and participation in practically any line of sporting activity one might desire. These opportunities were not, in my opinion, so readily available to my civilian colleague.

There is to-day a marked tendency to specialize. The general duties officer, who is the backbone of the branch, will, however, persist, and it should be his aim to become a first-rate doctor as well as a first-rate officer.

Every general duties officer should have a course in administration.

There should be closer co-operation between the general duties officer and his civilian counterpart.

Every general duties officer should do spells in one of the bigger hospitals.

The promotion course should be re-instituted. Short post-graduate courses of, say, a month in general surgery and medicine are, in my opinion, of doubtful value.

Unless he wishes to take up some other subject, he must endeavour to become an expert in Naval and Military hygiene and administration, though this should not be at the expense of his knowledge of classical medicine.

**Surgeon Lieutenant G. Pollitt:** The medical officer in the Services has very often to be his own clinical pathologist and specialist, because units of the Fighting Services are often stationed many miles from the nearest town, or are in ships at sea. Also in Service Medicine, medical officers often spend a considerable amount of time attached to small ships or units where the clinical material is slight.

Post-graduate courses should be particularly designed as refreshers in general medicine as applied to service age-groups, with a short course in clinical pathology, with special reference to microscopy.

In the Services the great majority of medical officers are attached to units, some large, some small, but all containing a large percentage of theoretically healthy individuals. The result is that the clinical material, as already mentioned, is slight. Acute cases are usually discharged to hospital, often some miles away, with the result that it is difficult for the unit medical officer to follow up his cases. The obvious answer to this is that all medical officers should do a spell in hospital every few years. However, Service hospitals must carry their specialists, as in the case of civilian hospitals. Medical officers with higher qualifications are the obvious choice for the specialist appointments, and officers with higher qualifications are therefore going to keep the hospital jobs permanently filled, with the exception of a few junior appointments, or else they are going to spend a considerable time attached to small units with little outlet for their accomplishments.

**Wing Commander G. Gilchrist:** The doctor who elects to make the general duties branch of one of the Services his permanent career will find that he is dealing, in the main, with a body of fit young adults, and that the work is, in fact, mostly preventive medicine. Secondly, as he progresses up the tree of promotion, his work will steadily become more administrative, and less clinical. But, and this is important, although he is becoming an administrator, he is still dealing in preventive medicine, and is now responsible for a far wider field than when he was a practitioner. He is, in fact, becoming a specialist of preventive medicine, in his own right and within his own general duties branch.

At this point, the budding young general duties specialist must have available the same opportunities to improve his knowledge and worldly position as are available to his colleagues of the specialist branches. He must know that if his record is good, he has a reasonable chance of study leave for the purpose of taking higher qualifications in the field of preventive medicine, for example, the D.P.H. or the D.T.M. & H., or there must be available to him senior courses in administration and staff duties. The obtaining of a diploma, or of a good pass mark on a course, must carry with it the prospect of financial advancement in the form of a gratuity or antedate in promotion. The antedate should also be much more freely used than is the practice to-day, and should be awarded to men with a steady record of reliable and meritorious service. An excellent time for a review of possible antedates would be at

those times when an officer normally becomes due for his periodical increments of pay. This would prove an excellent stimulant for those officers who had, up to that time, appeared to receive no special appreciation of good and faithful service.

There remains one other way in which a general duties medical officer may specialize within his branch. He may adopt, as his main interest, the medical aspects of the many scientific problems of the particular service to which he belongs, as, for example, the highly specialized subject of aviation medicine. In the Royal Air Force there exists the Institute of Aviation Medicine, established for the purpose of research and training, and to this Institute, officers who have shown a particular flair for the problems of aircrew may be attached for courses.

One last aspect of the problem must be touched on. The general duties medical officer feels that by the time he becomes due for retirement, he will have forgotten most of his professional knowledge, whereas the specialist has remained up to date throughout. On retirement posts must be available to the general duties officer under the National Health Act, when the time comes for him to hand up his uniform for the last time.

It is essential that a good type of volunteer practitioner be recruited to the general duties branches of the Services, and to achieve this, the Services must be able to offer as good chances of advancement as are available to the specialist branches of medicine. The existing belief that a medical officer all too rapidly becomes a "pen-pusher" must be dispelled. In order to attract men to this life, the domestic and financial position must be at all stages advantageous as compared with life in general practice.

**Wing Commander O. M. Fraser:** *The professional future of the General Duties Medical Officer.*—It is difficult to find answers to the objections raised by young medical officers to a career in the Service but I suggest that some of the following measures might make Service Medicine more attractive:

A posting to a Station should be for a definite minimum time, to enable the medical officer to get to know the people and the place, and to feel he is part of the Station and not just placed there temporarily.

He should be encouraged to meet the local practitioners and take part in their work, and also to visit hospitals in the vicinity.

For those who have started to specialize by resident hospital appointments in civil life but are not specialists in the Service, a grading as "expert", that is a G.D. medical officer with more than average knowledge of one aspect of medicine, and who is able to give expert advice on that particular subject.

An Officer who is recognized as "expert" should be given a short period of leave at regular intervals to attend hospital or specialized institution of his own choice to keep up to date in his subject—say, a month every two years or so. These officers will, of course, be eligible for study leave, as all are, to prepare for higher qualifications.

Each G.D. medical officer should do a spell of duty in a Service hospital, say, six months every five years, and if suitable be given the opportunity to become a specialist.

A period of leave might well be given to all officers to spend as assistants to a general practitioner. This would open to them a field of medicine which they rarely enter in Service Medicine.

Arrangements should be made to aid retiring Service M.O.s to find suitable posts in Government departments and industry, if they do not wish to take up general practice.

**Group Captain J. B. Gregor:** Some of the duties which are now undertaken by a qualified medical officer on a unit should be relegated to medical "other ranks" under the supervision of the unit medical officer. Much more of the unit medical officer's time should be given to matters of medical policy, both on the prevention and treatment sides. By this means, better careers will be given to the "other ranks" and trivial duties now assigned to unit medical officers will be done by them. A much higher standard of professional skill will therefore be maintained by the unit medical officer.

From the Service point of view it is essential that a general duties type of medical officer, from amongst whom most of the senior medical administrative officers will normally come, must be physically and mentally virile throughout his career and, therefore, on the average should be retired at a comparatively early age.

He must be well versed in his professional duties, both in general medicine and in medicine as particularly applicable to the Service, and he must be a good Service officer. To obtain the right man for this career, the individual must be offered adequate facilities for post-graduate study suitable to his rank, age and experience, at frequent intervals throughout his Service career. His pay, allowances and promotion must be always a little ahead of other branches.

It must be remembered that the medical officer, having a civilian qualification without which he cannot practise, has a position in the Service which is quite different from that of any other serving officer. He is not infrequently faced with personal and intimate problems on the psychological side connected with his superiors in the Service, and is the one officer who can give advice tantamount to an order to a superior officer. He must, therefore, be a good doctor and a good officer, and must have good pay and good prospects.

The objections to early retirement are that although better careers are given to the serving medical officers retirement is likely to take place just when expenses in educating children, &c., are high.

Pensions, therefore, must be reasonably adequate, and professional skill having been maintained, opportunities for obtaining appointments either in general practice or in medical administrative departments within the National Health Service should not prove difficult to obtain.

**Wing Commander J. L. Walsh:** For a medical officer to derive the maximum benefit from his Service career and give of his best to the Service, he must be a specialist in his own Service and in medicine as applied to that Service.

He must identify himself completely with his Service and consider himself an integral part of it, and his clinical knowledge must be maintained at the highest possible level.

To obtain these conditions, I make the following suggestions, which will, of course, be applicable to the situation as it exists in the Royal Air Force:

In addition to training selected medical officers to full operational standards of flying, reintroduce a modified flying course for all medical officers and award those who successfully complete this course a flying badge of special design.

Increase the number of vacancies available for medical officers on the courses at the various staff colleges.

Endeavour to increase the clinical material available to each general duties medical officer.

To implement the first suggestion, the bare reintroduction of a modified flying course for medical officers on the pre-war model would be insufficient. All medical officers whose medical category reached the necessary standard should be encouraged to take the course, and all those wishing to qualify for the modified flying badge should be given every opportunity to do so and subsequently to keep in flying practice if successful.

To increase the clinical material available, it is suggested that rather than a small sick quarters with one or two medical officers on each Station, the medical facilities of a number of Stations suitably placed geographically might be concentrated on one of these Stations in the equivalent of a small health centre or hospital. As the Services are now offering full treatment to the families of serving personnel, these centres should be equipped to afford in-patient and out-patient treatment to women and children.

A medical inspection and treatment room should be established at each of these Stations, staffed by two nursing orderlies. Each morning, medical officers from the centre should visit the surrounding Stations for sick parades, sanitary inspections and such other matters as require their attention.

This would necessitate a departure from the present practice of maintaining a medical officer on the station when flying is in progress, but it is submitted that with a medical officer available at the centre at any hour of the day or night, there should be no great delay in an emergency.

A further development would be the establishment of a medical administrative post at each centre, to be filled by a commissioned medical Warrant Officer or Senior N.C.O., who would relieve the medical officers of the routine administration. This arrangement would enable them to devote more time to the clinical side and would enlarge the scope and opportunity for commissioning of medical airmen.

**Group Captain J. Parry Evans:** The young Regular medical officer who is responsible for a Royal Air Force Station will find that on the average there will be a population of 1,000 to 1,500 consisting chiefly of Service personnel and their families. Although not responsible for the sanitation of the Station, he is the expert adviser on this subject. He has a Station sick quarters, with emergency surgical equipment and a few beds where he can detain and treat such cases as are within his competence.

The aircrews are very dependent upon the medical officer who must know them intimately. Aircrews have to be kept literally "fighting fit". Signs of staleness or fatigue can only be spotted in the early stages by an astute clinical observer. The ground personnel can be likened to factory workers, in so far as the workshops and hangars are concerned. Here is industrial medicine in all sorts of guises from mechanical hazards to poisonous metal plating processes.

After a few years of this type of professional life at home or overseas, a G.D. medical officer will decide whether he will continue on these lines and eventually become a medical administrator or whether he will concentrate on one of the accepted professional specialities.

The President said that he had been asked to give a summary of the discussion. It would be appreciated that this would not be easy after so many speakers, and he would also find it difficult to avoid expressing his own opinions.

The question was how the G.D.O. could be assisted so that the Services got the best value out of him and at the same time gave him due opportunities and also left him in an efficient state professionally when he retired.

A number of the speakers had made suggestions directed to training the G.D.O. to become a specialist. Their problem would not be solved by training all G.D.O.s to be specialists, though the good man should be able to get his chance: he ought generally to be able to make it for himself.

But the G.D.O., like the G.P., represented the average non-exceptional bulk of the profession. He could be fully efficient in his own sphere but he was not the standard of the specialist. In any case the Services must have G.D.O.s.

They had undoubtedly been neglected in the past, and something more should be done. The opinion that they should start with a period in hospital was general: the value of this experience was greatly increased by the recent wise decision to admit civilians to Service hospitals.

Subsequently, repeated courses should be arranged, not directed to training as a specialist but to training and refreshing in the duties of a G.D.O. There should also be postgraduate courses. In the past the G.D.O. has had too little stimulus to maintain his interest. It should be possible to arrange some reward or recognition for a good G.D.O. while he still remains in that position. It has been suggested by more than one speaker that the G.D.O. is the natural source of administrative officers, but in his, the President's, experience the most efficient administrators have been specialists.

The routine character of the duties of the G.D.O. had been mentioned by several speakers. Everything should be done to avoid stagnation, but the G.P. and other professions are in the same position. If a unit M.O. was overworked it was usually his own fault; cutting down the attendance at sick parades was a matter of knowing how to handle men, though a high rate may be the fault of the O.C. and not of the M.O.

A difficult matter was the insecurity of service of the G.D.O. and his rights of retiring.

He thought that conscription of doctors was unavoidable under the present law, for if medical students were called up before or during their medical training it would have a disastrous effect.

In conclusion he again warned the meeting against the fallacy of supposing that all G.D.O.s could become specialists.



## Section of Laryngology

President—E. COWPER TAMPLIN, M.C., F.R.C.S.Ed.

[May 6, 1949]

### STENOSIS OF THE LARYNX<sup>1</sup>

V. E. Negus: Traumatic stenosis may be due to a foreign body, to contusion, or to incised or penetrating wounds. The type of injury caused by a fall on the larynx is uncommon. Incised wounds are usually caused by razor cuts. Penetrating wounds, from fast-travelling missiles, usually kill the patient. One of the causes of stenosis is a high tracheostomy, and in one or two of my cases the first thing required was to remove the tube from a high position to a lower. The misplaced tracheostomy tube is a common cause of stenosis. Personally I use the word "tracheostomy" because I think it correct; the word "tracheotomy" means opening the trachea and closing it again, as for removing a tumour, but if a permanent opening or window is made I think the operation ought to be called "tracheostomy".

Foreign bodies are a very uncommon cause of permanent stenosis. Acute laryngitis I have seen as a cause once in an elderly patient who later developed carcinoma of the larynx, not long after the resulting cicatricial stenosis had been operated upon. One of the cases had perichondritis following tracheostomy but not caused by it, and another had stenosis following diathermy; I have seen other cases of the same type. Stenosis as a result of operation for malignant disease I have seen only once or twice; there may be contraction after laryngofissure.

These, I think, are the common causes. One must include also the paralytic cases, usually following operations on the thyroid gland.

As for treatment, it is possible to try continuous dilatation by putting a rubber core mould into the larynx, but I do not think the results are good. Generally speaking, the right treatment in my experience is the opening of the larynx by the ordinary laryngofissure route; all scar tissue should be removed and a plastic tube put in together with a skin graft applied to all raw surfaces. In cases where the glottis is affected a triangular tube is used.

The first patient shown to-day had to have the larynx reopened a week after operation because the X-rays showed that the tube was not in a good position; it must be in exact position if a proper result is to be obtained.

The length of time the tube should stay in varies. The shortest time in my experience was in a boy who fell off a bicycle; his tube was in position for twelve days. If, however, there is much destruction of cartilage, then permanent dilatation has to be kept up for a long time, even up to four months. Plastic tubes are very much less irritating than rubber and can be kept in for some months. I do not know that rules can be laid down as to how long the tube should remain in position.

Having talked about cicatricial stenosis and put forward the view that the right method of treatment is by external operation, with restoration of the lumen and the insertion of a skin graft, supported by a tube, I should like to refer to cases in which that is not suitable. If the larynx has been narrowed very much by cicatrization more harm than good might be done by operation. I would put it forward that in certain cases with marked destruction retention of the tracheostomy tube is best.

One of the patients who was shown has a very narrow glottis, but he can earn his living as a labourer, doing hard and dangerous work demolishing buildings, and he has quite a good voice. One has to consider how best to give the patient a good clear voice and free respiration. If one can get rid of the tube altogether so much the better; if not, it is very important to use a correct tube. I think it should be a shade shorter than the Jackson tube and longer than the Edinburgh pattern.

I remember composing a paper on this subject and asking Sir StClair Thomson to criticize it before I went to America. I said in the paper that wearing a permanent tracheostomy tube was no worse than wearing a denture, but Sir StClair pointed out that it was much less trouble, because a denture had to be cleaned every time after eating but a tracheostomy tube need be cleaned only once a day.

Patients appear with the recurrent nerves paralysed and the cords lying quite close together so that it is impossible to breathe properly. So far I have treated these cases—partly because

<sup>1</sup>Before proceeding to open this subject Mr. V. E. Negus demonstrated a number of patients to illustrate various types of abnormality and methods of treatment.

After a few years of this type of professional life at home or overseas, a G.D. medical officer will decide whether he will continue on these lines and eventually become a medical administrator or whether he will concentrate on one of the accepted professional specialities.

The President said that he had been asked to give a summary of the discussion. It would be appreciated that this would not be easy after so many speakers, and he would also find it difficult to avoid expressing his own opinions.

The question was how the G.D.O. could be assisted so that the Services got the best value out of him and at the same time gave him due opportunities and also left him in an efficient state professionally when he retired.

A number of the speakers had made suggestions directed to training the G.D.O. to become a specialist. Their problem would not be solved by training all G.D.O.s to be specialists, though the good man should be able to get his chance: he ought generally to be able to make it for himself.

But the G.D.O., like the G.P., represented the average non-exceptional bulk of the profession. He could be fully efficient in his own sphere but he was not the standard of the specialist. In any case the Services must have G.D.O.s.

They had undoubtedly been neglected in the past, and something more should be done. The opinion that they should start with a period in hospital was general: the value of this experience was greatly increased by the recent wise decision to admit civilians to Service hospitals.

Subsequently, repeated courses should be arranged, not directed to training as a specialist but to training and refreshing in the duties of a G.D.O. There should also be postgraduate courses. In the past the G.D.O. has had too little stimulus to maintain his interest. It should be possible to arrange some reward or recognition for a good G.D.O. while he still remains in that position. It has been suggested by more than one speaker that the G.D.O. is the natural source of administrative officers, but in his, the President's, experience the most efficient administrators have been specialists.

The routine character of the duties of the G.D.O. had been mentioned by several speakers. Everything should be done to avoid stagnation, but the G.P. and other professions are in the same position. If a unit M.O. was overworked it was usually his own fault; cutting down the attendance at sick parades was a matter of knowing how to handle men, though a high rate may be the fault of the O.C. and not of the M.O.

A difficult matter was the insecurity of service of the G.D.O. and his rights of retiring. He thought that conscription of doctors was unavoidable under the present law, for if medical students were called up before or during their medical training it would have a disastrous effect.

In conclusion he again warned the meeting against the fallacy of supposing that all G.D.O.s could become specialists.

A smear of mastisol on the mould, allowed to become tacky, may be employed to assist in the application of the graft to the mould. This, I think, is preferable to fixation by stitches or ligatures.

(3) *Insecure fixation and insufficiently long retention of the mould.*—These are very closely interrelated. Free skin-grafts have an extraordinary tendency to contract with astounding rapidity. In the very early days after the 1914-18 war we learnt our lesson on this subject by bitter experience. The mould from a beautifully grafted buccal sulcus would be removed for inspection fourteen days after operation and the case sent to the dental department for the preparation of a temporary prosthesis or denture. Whilst the patient was kept waiting for attention for even less than an hour contraction would occur sufficient to prevent replacement of the original mould. The grafted eye socket often behaves in similar fashion.

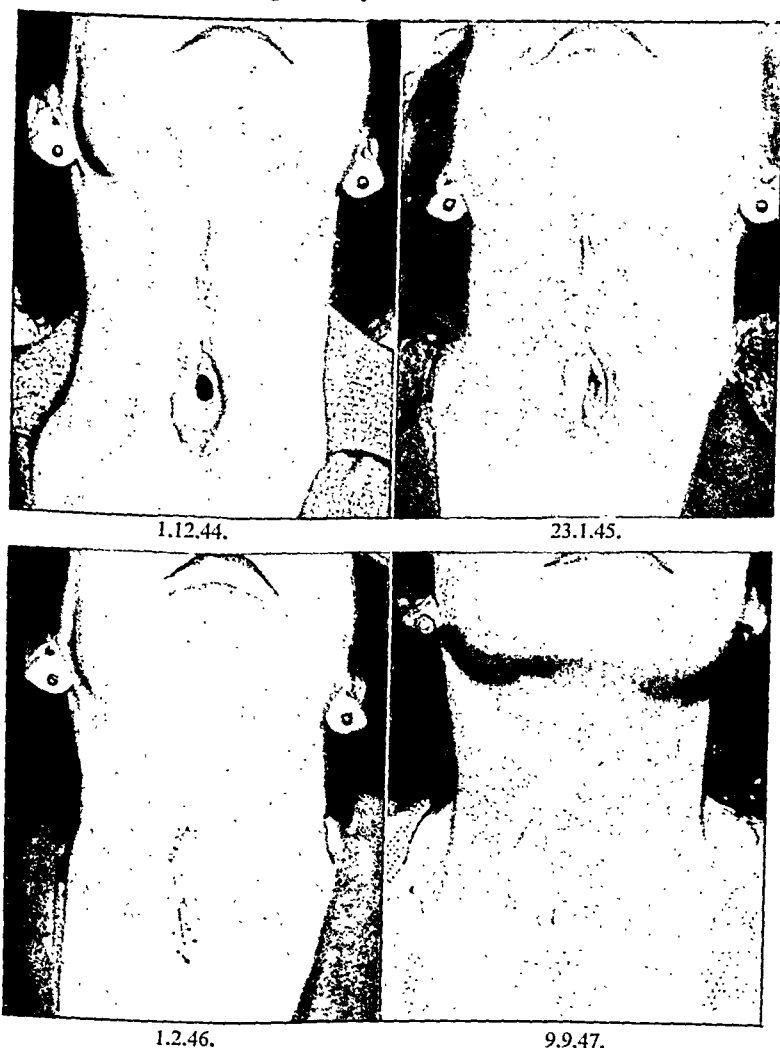


FIG. 1.—Laryngeal stenosis following motoring accident. Three previous operations, performed at thirteen, twenty-six and twenty-seven months after injury, had failed to relieve obstruction. Successful result followed closed grafting procedure three and a half years after injury.

It is essential to maintain constant elastic pressure on the grafted area and it must be obvious that this is easier, as Figi has put it "within a closed tube than in one that has been laid open". For this reason there can be little doubt about the advisability of closing the external wound over the graft-covered mould. In none of my cases was successful grafting achieved when the wound was left open. The mould was extruded early and subsequent

of my early association with Sir StClair Thomson—with a suitable tracheostomy tube and find that they live a comfortable life and speak normally. I should be delighted to be converted to operations on the airway if I knew that the result would provide a clear voice and free respiration in the absence of a tracheostomy tube.

**T. Pomfret Kilner:** *How Soon After Stenosis is Established Should Treatment be Instituted?*<sup>1</sup>

Since the patient with a tracheostomy can continue to breathe and live almost indefinitely, the treatment of the stenosis above the tracheostomy need never be considered an urgent affair. The need for constant toilet of the apparatus is, however, troublesome; the expulsion of mucus from an unnatural and obvious opening on the skin is unpleasant and unæsthetic; the often noisy breathing through this opening is unpleasant and difficulty in speaking is inconvenient. Furthermore, the constant wearing of a tube must produce irritation and be the cause of a low-grade tracheitis. Presumably, too, the regular inspiration of unwarmed and unmoistened air may predispose to pulmonary complications. There can be little doubt, therefore, that the sooner a natural state of things can be restored the better from all points of view.

It would seem reasonable to assume that a state of quiescence has been reached three months after cessation of acute symptoms, whether caused by inflammation or injury. Six months should be ample to ensure this. In my cases the first attempt at restoration of lumen was made four years, six years and just over one year respectively after the initial inflammation or injury. In all, the stenosis recurred very soon after the skin-grafting procedure. It is likely that some or all of the following factors share the blame for this failure.

(1) *Insufficiently radical excision of well-organized scar tissue.*—It is natural perhaps for the plastic surgeon to be haunted by fear of penetrating the wall of the air passage: I imagine that many expert otorhinolaryngologists work under a similar strain. Good lighting, efficient suction and anxiety-free anaesthesia are essential if full exposure and removal of the cause of obstruction are to be achieved.

The surface left after excision should be smooth: all irregular tags or projections must be trimmed flush with the surface. There must be no loose edges of scar or mucosa at the upper or lower extremities of the raw area, for these tend to produce shelf-like projections which, however effective the grafting, cause valvular obstruction.

(2) *Unsatisfactory grafting of the raw surface.*—*The graft:* This should be ample in dimensions to more than cover the raw surface. It should be thin and hairless and is best taken from the inner aspect of the upper arm, preferably the left arm in a right-handed patient.

*Method of application of the graft to the raw surface:* The nature of the "form" on which the graft is applied does not appear to me to be of great importance provided it succeeds in applying the graft snugly to its bed and in preventing the accumulation of blood or serum between graft and raw surface. I think it should be as light as possible—for it always has a tendency to slide downwards.

Mr. Negus's plastic tube or triangular section is intriguing but I cannot think that it represents the best graft-conveyor for ordinary cases of stenosis. It may be indicated when an attempt is being made to reproduce something to replace the cords and it may be that when warm it is sufficiently pliable to adapt itself to the cavity in which it is placed.

I see no reason why the "form" should be tubular and indeed I think a solid form offers distinct advantages. The patient does not require an airway through the operation area and saliva, trickling down the tube into the tracheostomy, can be only a nuisance. It would be ideal, of course, if one could safely introduce and securely fix in position a graft-covered tube and completely close both operation wound and tracheostomy, and later remove the tube through the mouth, certain that no contraction would then occur. Until more certain methods of fixation have been devised and until we know more about the control of contraction in newly grafted areas, however, this must remain merely an ideal.

Sorbo sponge encased in a finger-stall should be excellent but the most satisfactory material revealed by my very limited experience has been pink dental wax. This is encased in a finger-cot and at body temperature moulds itself to any inequalities in the raw surface. *The form should extend beyond the raw surface both above and below: only in this way can shelf-like projections be avoided.*

Bateman's special tracheotomy tube does not represent an ideal "form" on which to apply a graft but it is a useful instrument in the after-treatment.

The mould, whatever its nature, should have a diameter larger than the normal diameter of the larynx. Over-correction to a reasonable degree should be the surgeon's aim.

<sup>1</sup> 17 lantern slides were projected illustrating original condition, measures employed and results obtained in three cases. Two of these cases were presented for examination earlier in the meeting and the photographic record of one of them is reproduced (fig. 1).

A smear of mastisol on the mould, allowed to become tacky, may be employed to assist in the application of the graft to the mould. This, I think, is preferable to fixation by stitches or ligatures.

(3) *Insecure fixation and insufficiently long retention of the mould.*—These are very closely interrelated. Free skin-grafts have an extraordinary tendency to contract with astounding rapidity. In the very early days after the 1914-18 war we learnt our lesson on this subject by bitter experience. The mould from a beautifully grafted buccal sulcus would be removed for inspection fourteen days after operation and the case sent to the dental department for the preparation of a temporary prosthesis or denture. Whilst the patient was kept waiting for attention for even less than an hour contraction would occur sufficient to prevent replacement of the original mould. The grafted eye socket often behaves in similar fashion.

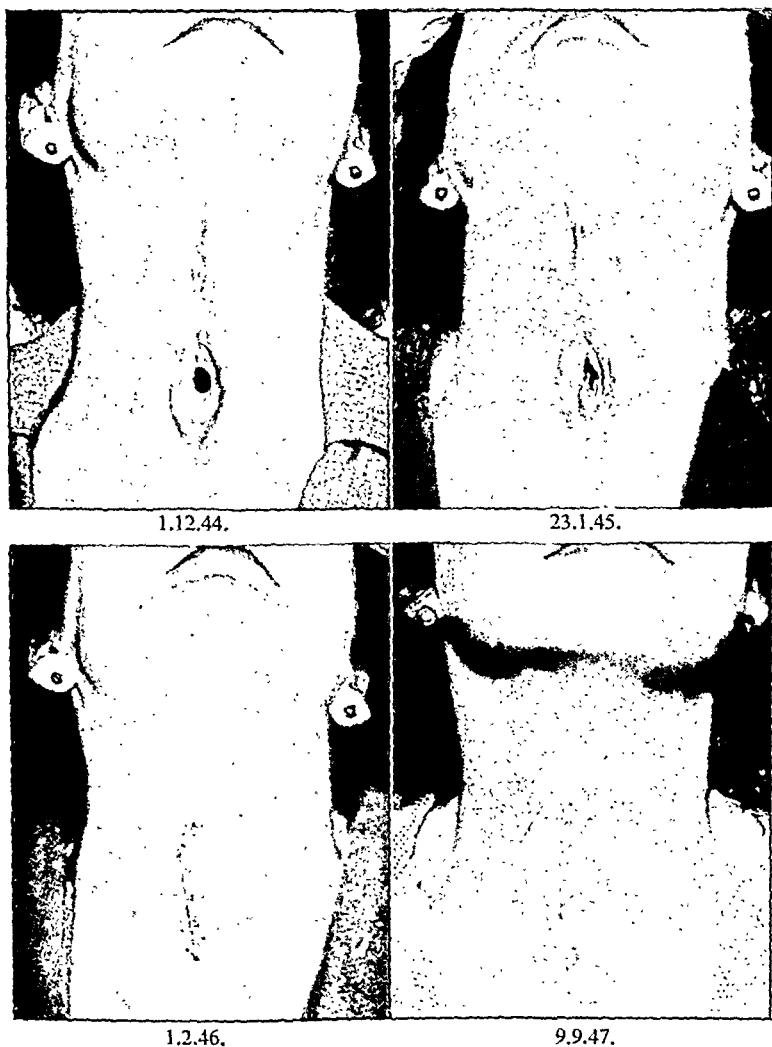


FIG. 1.—Laryngeal stenosis following motoring accident. Three previous operations, performed at thirteen, twenty-six and twenty-seven months after injury, had failed to relieve obstruction. Successful result followed closed grafting procedure three and a half years after injury.

It is essential to maintain constant elastic pressure on the grafted area and it must be obvious that this is easier, as Figi has put it "within a closed tube than in one that has been laid open". For this reason there can be little doubt about the advisability of closing the external wound over the graft-covered mould. In none of my cases was successful grafting achieved when the wound was left open. The mould was extruded early and subsequent

repeated packing proved ineffectual in preventing contraction. Closure of the external wound and early sound healing are then the most important aids to satisfactory grafting.

Such closure carries with it the necessity for securely fixing the mould, preventing it from sliding downwards when the tracheostomy tube is removed for cleansing or being forcibly expelled upwards during the attacks of coughing so commonly accompanying this necessary toilet. The transverse wire stitches of Schmiegelow always employed by Mr. Negus are the most satisfactory means of fixation. These should be reasonably thick and firm or they will break.

Fourteen days' retention of the mould is certainly not long enough. In one of my cases I planned to keep the mould in position for six weeks at least. The single wire fixation suture was too fine and too soft and broke on one side. The mould was discharged spontaneously through the mouth during a spasm of coughing on the twenty-second day and I think we were just fortunate that no material contraction occurred. The successful result of the operation probably depended on a good graft applied on an over-size mould which gave allowance for a reasonable degree of contraction.

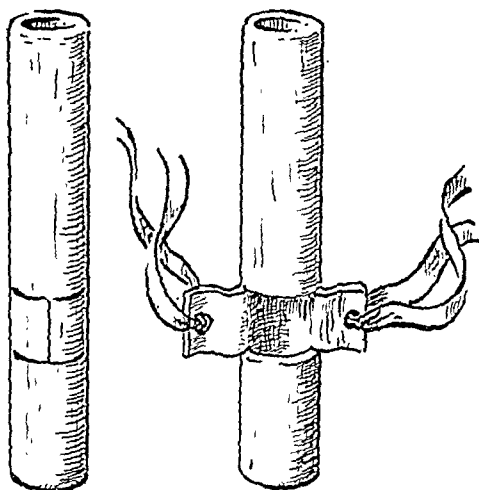


FIG. 2.—An extemporized tubular prosthesis employed in one case for the application of the graft.

(4) *Insufficient attention to post-operative treatment.*—If the mould can be retained in position for as long as six weeks, little subsequent contraction is likely to occur but this statement should not be trusted and careful and regular attention should be given to the case for several further weeks after operation.

The routine treatment for surface free grafts, starting two to three weeks after operation, is grease massage of a rotatory character. This may be imitated in the larynx by the regular passage of a bougie of ample size, well lubricated with liquid paraffin. Any commencing contraction will be noted and steps taken to counteract this by regular intermittent dilatation continued until that unpredictable contractile period is safely passed. In some cases continuous dilatation by an indwelling bougie, or by some instrument following the design of Bateman's tube may be indicated.

(5) *Insufficient attention to general condition and repetition of operations with insufficiently long intervals.*—Patients calling for this treatment have commonly passed through very exhausting illnesses or experiences. They require "building up" both physically and psychologically before the kind of operative interference under discussion is attempted.

Ideally, only one operation should be required and more successful results will be obtained if we school ourselves to meet all the requirements I have mentioned; but just as surface grafts, e.g. on burnt eyelids, will contract, so contraction in this difficult region must be expected to occur in some patients and this, although disappointing, should not be allowed to dishearten either patient or surgeon or on the other hand produce the kind of panic which leads the surgeon to make another attempt before the tissues have been given ample time to settle down completely.

John F. Simpson described a case of complete subglottic obstruction following high tracheotomy. The patient requested the closure of the tracheotomy. By an external operation a new airway was fashioned, the remnant of one cord and the anterior part of the cricoid ring being removed. An

angulation prevented the use of a straight tube, as described by Mr. Negus, for canalizing the larynx and trachea. Dental stent was used to make an accurately fitting obturator to carry the Thiersch graft. Owing to discomfort the larynx was partly reopened on the eighth day and the mould removed when the graft was seen to have taken successfully, an interesting fact in view of the six weeks recommended in the preceding discussion as being necessary for the retention of the mould. It was certain that this case could not have succeeded without the administration of penicillin.

Post-operative treatment consisted in the passage of gum elastic œsophageal bougies that could pass round the bend present at the junction of the larynx and trachea. The tracheotomy opening was closed some weeks later. Mr. Simpson played a gramophone record of the voice before and after operation, and stressed the importance of speech therapy in the after-treatment of such cases.

Mr. Simpson then referred to cases of bilateral abductor paralysis (paralytic stenosis). Although several surgeons had started to operate on these cases in this country he thought that Mr. Brian Reeves' case and his own two cases were the first to be shown to the Section which had undergone extralaryngeal arytenoidectomy. The two cases he showed were operated on according to the method of De Graaf Woodman of New York who described his modification of the extralaryngeal arytenoidectomy in the *Archives of Oto-Laryngology*, January 1946 (Vol. 43, p. 63), and in the *Annals of Oto-Rhino-Laryngology* in September 1948 (Vol. 57, p. 695).

Briefly, the operation consists of a preliminary tracheotomy after which a bronchoscope is passed until it makes contact with the tracheotomy tube. The bronchoscope steadies the arytenoid cartilage while it is being removed submucosally. The posterior edge of the thyroid cartilage is exposed by an incision along the anterior border of the sternomastoid. The alar cartilage is raised from the perichondrium on its mesial surface. After dividing the superior cornu and disarticulating the cricothyroid joint the alar is conveniently retracted outwards by a gauze strip, and it is then possible to cut down on the external surface of the arytenoid and to shell it out submucosally. The dissection can be facilitated by encircling the arytenoid with a traction loop. When the vocal process comes into view a chromic catgut stitch is placed around it submucosally, so that it and the posterior part of the cord can be pulled outwards. The arytenoid cartilage is then removed except for its vocal process. The stitch tethering the vocal process is then tied round the inferior cornu so as to brace the cord in the abducted position, which can be checked as the bronchoscope is withdrawn. The tracheotomy tube is removed within a week and the patient can leave hospital in a fortnight.

The patients shown were now able to walk upstairs. Mr. Simpson claimed that one of his patients had as good a voice as Mr. Negus's patient with the tracheotomy and valve. Even when a somewhat husky voice results it seemed to him that this operation was preferable to a tracheotomy.

Victor Riddell spoke as a general surgeon with a special interest in thyroid surgery. Bilateral injury to the recurrent laryngeal nerves was one of the causes of stenosis of the larynx.

There were two points he wanted to make:

#### Identification of the Recurrent Nerves

First in his opinion the "blind" operation of thyroidectomy was obsolete—by that he meant thyroidectomy without identification of the recurrent laryngeal nerves. Two advances in recent years had made this point of view possible, namely the general improvement in anaesthesia, and the introduction of the antithyroid agent thiouracil by means of which it was possible to convert the toxic into the non-toxic goitre before operation. The combined effect of these two advances had been to reduce the necessity for speed in operating as patients were no longer constitutionally so ill at the time of operation as they were in the days before they could be prepared with thiouracil. It was in their power to make the patient safe for surgery: it remained only to make surgery safe for the patient. To-day an unhurried operation could be carried out. Surgeons could—within limits—with safety take their time and in all cases not only identify the inferior thyroid arteries and the parathyroid glands, but also both the recurrent laryngeal nerves.

In the last 500 thyroid lobectomies he had carried out he had done the "blind" operation in 400, and exposure of the recurrent laryngeal nerves in the last 100. He had not yet determined the number of vocal cord palsies as a result of the blind operation, but he suspected that in his hands it was 6 to 8%, and therefore presumably in the hands of occasional thyroid surgeons 10 to 15%. In the 100 cases where the recurrent laryngeal nerves were identified there had been no instance of vocal cord palsy. Clearly this happy issue could not be expected to last, but it was sufficiently convincing to encourage them to continue with the exposure of the nerve.

#### Laryngoscopy, Pre- and Post-operative

Second a routine pre-operative and post-operative laryngoscopy should be done before and after every thyroidectomy.

Pre-operative laryngoscopy occasionally revealed a paralysed cord; in some instances this might influence the surgeon's decision to operate, and in others would exonerate him if symptoms developed subsequent to operation.

Post-operative laryngoscopy was essential if a true estimate of the frequency of vocal cord damage following thyroidectomy was to be obtained. In his experience vocal cord paralysis following thyroidectomy was far commoner than was supposed. So far as he knew, existing statistics, including those of the Lahey Clinic, were based on the selective post-operative examination of vocal cords in those patients only who had hoarseness of voice or other obvious symptom of recurrent laryngeal nerve damage. This system fails to reveal those cases of unilateral recurrent nerve damage in which symptoms are minimal as a result of rapid compensatory readjustment by the normal cord. There are a considerable number of such cases and there is the danger that it may be assumed that there has been no nerve damage unless we insist on a routine post-operative laryngoscopic examination in all patients who have had a thyroidectomy.

Brian Reeves showed slides to demonstrate the post-operative laryngeal appearances of the De Graaf Woodman operation.

In view of the gross post-operative laryngeal œdema he stressed the importance of a tracheostomy.

In the case he demonstrated (*vide infra*) severe laryngeal œdema persisted for fourteen days and it was not until twenty-eight days after operation that the œdema had subsided.

#### Bilateral Abductor Laryngeal Paralysis.—BRIAN REEVES.

Mrs. T., aged 52. 2.7.47: Larynx normal with movement unimpaired.

12.7.47: Partial thyroidectomy (Mr. R. Strang).

22.7.47: Larynx (post-operative) shows unimpaired movement.

14.9.48 (fourteen months after operation): Referred by private doctor with a six months' history of hoarseness and gradually increasing inspiratory stridor, worse at night.

*Physical examination.*—Bilateral abductor paralysis of the larynx with marked inspiratory stridor. Was kept under observation. Stridor became progressively worse. No other neurological signs.

16.11.48: Impending asphyxia.

17.11.48: Tracheostomy. External (right) arytenoidectomy with anchoring of cord in abduction to inferior cornu of thyroid cartilage (after De Graaf Woodman).

Tracheostomy was allowed to close forty-seven days after operation. Patient discharged hospital fifty-one days after operation. Now lives an almost normal life for a woman of her age. States that she would experience some distress if she were to run upstairs or indulge in energetic polishing of furniture. Has a husky voice.

I. Simson Hall said that there was quite obviously a conflict of opinion as regards the treatment of bilateral laryngeal paralysis. He wished to put in a plea that account be taken of the opinion of the patients. If the patients were sufficiently comfortable with a permanent tracheotomy, by all means let them keep their tubes, but in the operation which Mr. Simpson had described they had a great advantage over the others, and he thought that the patient's opinion should be considered.

W. A. Mill described two cases of subacute inflammatory stenosis. In each there was in the subglottic area what appeared to be an inflammatory swelling. The first case, in a doctor, settled down after tracheotomy, the evacuation of a little pus from the swelling and treatment by sulphathiazole. He was sure the case was one of perichondritis of the cricoid cartilage. He at present had under treatment a similar case in a woman. He had not met these cases otherwise and would be glad to hear if any member of the Section had met similar ones.

R. D. Owen asked Professor Kilner whether it was always possible to skin graft. He related the case of a young woman, aged 28, where he found it extremely difficult to dissect a satisfactory dry bed out of the scarred tissues in the neck, and where there was practically no cartilage left, due to the previous perichondritis. In this case he followed the late Professor Schmiegelow's technique, but using a wide-bored portex tube, suitably anchored by two strands of German silver wire, the cut ends of which were allowed to remain buried under the skin surface. The tube was left in position for five months. When it was removed the result was perfectly satisfactory, with a well-epithelialized airway and a reasonable voice. He quite realized, however, that skin grafting was the right procedure.

V. E. Negus, in reply, commented on the value of the discussion; it had brought out many points on which it was desirable to form conclusions. He himself had been stimulated in various directions. He had shown a number of cases in which he had attempted to form an adequate lumen, and had inserted a skin graft, but with inability to dispense with a tube. It might be that the technique was wrong, and that if he had had a plastic surgeon attached to his hospital he would have profited from his help. But he knew that one or two of the cases he had shown that day, although able to dispense with their tube, preferred to retain it. He could not subscribe to the view that it was a real hardship. A tube, if properly designed and fitted, was of very little inconvenience. It was difficult to predict which were going to be the successful cases.

An important question was that of surgical displacement of the arytenoid. It was possible that this would in time replace permanent tracheostomy.

If the patients with a tube had an expiratory valve their expectoration and cough were easy, and they coughed up the mucus as the ordinary person did; he was sorry to contradict Professor Kilner on that point.

Mr. Simpson had said that it was better to make the obturator fit the lumen. Personally he attempted to restore the lumen and make it straight.

Instead of a bronchoscope he would recommend a tracheoscope to fix the arytenoid cartilage.

In reply to questions, T. Pomfret Kilner said: (1) That he had found stent too heavy a material for use in the larynx: he preferred dental pink wax; (2) that systemic penicillin therapy, available for only his third case, had completely prevented inflammatory reaction; (3) that he considered it unsurgical to employ a mould without a graft. Schmiegelow had worked without graft and Russian surgeons had reported good results in contracted eye sockets obtained by similar means. Nevertheless, the best dressing for any raw surface was skin and it was asking too much of Nature to expect satisfactory spread of epithelium over the large raw surfaces he had encountered after excision of the scar tissue responsible for stenosis; (4) that his anaesthetists had sometimes employed the cuff intra-tracheal tube which provided added protection against inspiration of fluids during operation; (5) that he thought Mr. Negus made too light of the wearing of a tracheostomy tube; it could not be compared to the wearing of dentures and the aim of treatment should be to discard the tube and close the stoma.



## Section of Urology

President—TERENCE J. MILLIN, M.A., M.Ch., F.R.C.S.

[June 30, 1949]

### DISCUSSION ON CHRONIC RETENTION OF URINE

The President, in opening the Discussion, mentioned that it was difficult to define the term "Chronic Retention of Urine". Its meaning was perfectly clear, but its application varied. He suggested that they should confine themselves to the consideration of the atonic type of bladder—persistently retaining 15 oz. or more, often exhibiting an overflow at night—and renal impairment as shown by clinical, biological and radiological tests. They would discuss the treatment of such a case, the course to be followed and the final restoration of function.

Mr. Wilson Hey (Manchester): Ten years ago, in the pre-penicillin and pre-streptomycin days, I practised aseptic prostatectomy, and five years ago I published my results (Hey, W. H., 1945, *Brit. J. Surg.*, 33, 41). It may be as well to describe briefly the four groups of cases of chronic retention of urine:

GROUP I: Simple case of residual urine of 6 oz. or less, with no bodily disease and normal renal function.

GROUP II: Blood urea of under 80 mg. per 100 ml., residual urine of under 15 ounces, often infected urine and pyuria.

GROUP III: Residual urine 1 to 5 pints. Blood urea 80 to 200. Uræmic anæmia or vomiting is often present.

GROUP IV: Blood urea over 200, with evidence of cardiorenal failure, such as œdema and, on occasion, ascites.

Four reasons have compelled me, in about 2% of cases of chronic retention with renal failure, to return to slow decompression, but now I also employ antibiotics:

- (1) The reluctance of urologists to accept the highest standards of asepsis.
- (2) My determination to reduce the average mortality of 24% in my Groups III and IV cases.
- (3) The aid of penicillin and streptomycin.
- (4) The necessity to consider the needs of the general prostatectomist and not the specialist in any one type of prostatectomy.

The prostatectomist requires wide experience and a team—in fact the prostatectomy team is perhaps of as much importance as the prostatectomist himself. There is no place for the occasional prostatectomist, whether he be a general surgeon or a urologist.

*Chronic retention.*—In chronic retention, if the various types of operations produce mortalities which vary between 1% and 4% in the hands of the expert, any of these operations

must be suitable. Perurethral resection, however, requires long training and should be a whole-time job; it necessitates a surgeon with a mentality capable of putting up with a mortality of 15% in his first hundred cases. Enucleation, and prostatectomy to avoid the occurrence of malignancy in the future, are two very different operations.

A prostatectomy can be either aseptic, antiseptic or antibiotic. In chronic retention, with advanced renal failure, a combination of sepsis and antibiosis is the ideal. Both antiseptics and sulphonamides are harmful.

All cases of prostatic obstruction have some degree of chronic retention. If there are no signs of renal failure, then the one-stage prostatectomy, with sudden decompression, is essential, even if there are several pints of residual urine. With acute-on-chronic retention, prophylactic penicillin and streptomycin should be administered an hour before the operation. In the whole of Medicine it is only the surgeon who can fix zero hour—when the battle between him and the microbe should begin. He should imitate the Japs at Pearl Harbour by putting the offensive in full action by antibiotics an hour or two before the operational attack is made.

*Chronic retention with renal failure* is our only consideration in this Discussion; and one man may have this failure with 6 ounces of residual urine, whilst another man has good kidneys with four pints permanently in the bladder.

Although I hope that in the future only one operation will ever be done on the prostate, decompression may be either sudden or slow. The more confidence the surgeon has in his asepsis, the fewer will be the slow decompressions, because slow decompression means infection which has to be rooted out by antibiotics, and because slow decompression does not of necessity relieve renal pressure on account of the obstruction of the ureter produced by the prostate.

#### *Ureteral Obstruction*

In 1930 Rathbun attempted to prove ureteral obstruction by the benign prostate by means of pyelograms. My 1,200 sudden decompressions have given me many opportunities for investigating this ureteric obstruction still further. The ureter which normally runs for  $\frac{1}{2}$  in. obliquely through the bladder wall may with a hypertrophied, distended bladder have an intramural course of  $1\frac{1}{2}$  in. The ureters are often inserted high, with marked tortuosity above (shown by I.V.P.). After sudden decompression with excessive chronic retention the ureters are either "silent", or, if there is no obstruction, the urine dribbles away.

In my first series of experiments I passed a ureteric catheter into one renal pelvis and emptied the urine into a test-tube, and as much as 1 or 2 ounces were collected. After removal of the prostate one could frequently see the non-catheterized, hitherto "silent" ureter pouring out urine. It has always been a saying of mine that after sudden decompression spurting ureters are of good omen.

The next series of experiments was done with the help of a physicist and a mercury-manometer. In 30 cases of chronic retention of over one pint, all patients with evidences of some renal deficiency, I took pressures firstly of the bladder and then, about five minutes later, the pressure of each renal pelvis by means of ureteric catheters.

The average bladder pressure was 23.4 mm. of mercury. In 42 kidneys the renal pressure was raised to an average of 7 mm.—the highest being 15.5. In one case the ureter was impassable before the prostatectomy and passable afterwards. In 17 cases there was no renal pelvis pressure. In 15 patients both kidneys had a raised bilateral renal pressure; i.e. in 50% of all the cases.

To sum up: A suprapubic or catheter drainage would have incompletely relieved pressure in both kidneys in 50% of cases, and in 71% one kidney would not have been completely relieved. Therefore, slow decompression, although relieving bladder pressure, does not necessarily relieve renal pressure. Hence, the sooner the prostatectomy, with its trigonectomy, is done the better.

I am not suggesting that these experiments are entirely satisfactory but they do show trends. I do not recommend a repetition of these experiments because I do not think that the passage of a ureteric catheter is free from risk.

#### *Slow Decompression*

A sudden decompression is a shock, like anything else sudden, to an old man; and although it produces congestion of the bladder wall, without sepsis it does not produce the blood-blocked ureters and kidneys that we have seen in the presence of sepsis. I now slowly decompress in 2% to 3% of cases, with penicillin intramuscularly, protamine-zinc-insulin and adrenaline deeply subcutaneously, and streptomycin (1 : 1,000) preferably locally, but if intramuscularly, about  $\frac{1}{2}$  of a gramme every six hours to 1 to 2 grammes. The decompression, if the urine is purulent, should be by the in-dwelling catheter, and if aseptic by a

minute suprapubic tube, best exemplified by Riches (1943). The decompression should be extremely slow at first, increasing later with great rapidity. It should be done hourly for perhaps two days and at the most three days. Sufficient streptomycin should be injected into the bladder to keep the urine roughly at the strength of 1 : 1,000; i.e. a 2-pint bladder needs 1 gramme of streptomycin at the first decompression. This has reduced my mortality in Group IV, which was 66%, to 14.3% in 14 cases, and in my Group III, which was 16%, to 6.2% in 32 cases.

The prostatectomy should be done in three days at the outside if the patient is fit; and the condition of the patient, the tongue and the urine are of more importance than the renal function tests.

It is difficult to assess an acute-on-chronic retention, and each case must be judged on its merits. An acute-on-chronic retention with vomiting may have a blood urea of over 400 and recover, but with simple chronic retention I have never succeeded with a blood urea of over 300.

In these cases of chronic retention with renal failure, cancer need not be considered as it should in all other cases. Therefore the simplest procedure is the best, whether it is enucleation or perurethral resection at one or more sittings.

Without renal failure cancer must be suspected; a total prostatectomy and not an enucleation should be performed.

With high uræmias, transfusion with liquid plasma before operation is essential. Dried plasma should not be used. Blood transfusion at times may be dangerous, and sulphonamide therapy in the presence of renal failure should be abandoned.

After operation, the patient should be given a rectal drip, or, if the case seems critical, an insulin-adrenaline-glucose drip (ordinary insulin 30 units, adrenaline 15 minims, glucose 5% to the litre), alternating, if desired, with sodium sulphate.

*Retention in cancer.*—Lastly, in chronic, or acute-on-chronic, retention in cancer, or even dubious cancer, a testicular evisceration under pentothal, and intramuscular and oral oestrogens in massive doses—up to 100 mg. a day—will sometimes work wonders. They are far better than catheters and may allow of a safe prostatectomy days, or even weeks, later.

A permanent suprapubic drainage is a confession of failure, and a misery to the patient, and should be abandoned.

#### REFERENCES

- RATHBUN, N. P. (1930) *J. Urol.*, 25, 23.  
 RICHES, E. W. (1943) *Lancet* (ii), 128.

Mr. E. W. Riches (The Middlesex Hospital): Enlargement of the prostate is the most frequent cause of chronic retention. In the prostatic patient chronic retention comes on slowly; the term "chronic" implies that the condition has been present for a long time, but as the duration is unknown when the patient is first seen we may define chronic retention as being relatively painless in contrast with the sudden painful onset of acute retention. Acute retention may be superimposed on chronic, especially in the prostatic patient who is confined to bed for some intercurrent illness such as cardiac failure; in such a case the giving of mercurial diuretics is often the deciding factor in overfilling the bladder. Chronic retention does not imply any specific amount of residual urine nor any particular degree of renal damage, although both are usually present. Its recognition demands the ability to detect a full bladder and this is not always easy in a fat patient.

Urinary complaints may be minimal and the main symptoms may be general ill-health, loss of weight and alterations in the sense of taste, symptoms of uræmia which mimic those of gastro-intestinal disease.

The degree of renal damage is probably of greater importance than the presence of infection although the two are interconnected. It is therefore necessary to make some estimate of it before embarking on treatment. Whilst the blood urea gives a safe and quick indication of renal function it is not always reliable, and it should if possible be supplemented by some other test. It is usually possible to obtain a specimen of urine from the overflow and the presence of albumin in the absence of gross pus suggests renal damage; if sufficient urine can be obtained for an estimation of specific gravity this should also be done; a fixed sp. gr. of 1010 is of serious import. The alkali reserve and plasma proteins and chlorides should also be estimated as they give an indication of the kind of intravenous therapy which may be needed.

If it were possible to detect which cases have dilated ureters and renal pelves the problems of treatment would be easier, but in the presence of serious renal damage an excretion pyelogram is neither informative nor safe as the dye is not excreted.

## TREATMENT

The bladder should not be immediately emptied just because it is found to be full. The condition has probably existed for some time and a further delay of a few hours or even a day is less harmful than a hasty operation with incomplete investigation or preparation. It is remarkable how well these patients remain until someone interferes with them.

The chief differences of opinion centre around the need for preliminary drainage, and the method to be used. I am firmly of the opinion that drainage is necessary in most chronic cases, that sudden decompression should be avoided and that drainage should be done in such a way as not to prejudice the subsequent prostatectomy.

*The Need for Drainage*

In order to avoid the introduction of too many variable factors I will give the figures of one operation only, retropubic prostatectomy. Out of 321 cases, benign and malignant, 117 were operated upon in two stages and 204 in one stage. Of the 117 two-stage cases 93 had chronic retention, the remaining 24 being drained for other reasons. There were 5 deaths, a mortality of 4.2%. 4 of the patients with chronic retention died, one from uræmia, one from cerebral thrombosis, one from pulmonary embolus, and one from heart failure. The fifth death was from pulmonary embolus. Thus the mortality in the cases with chronic retention was 4 out of 93 or 4.3%. Drainage was by suprapubic catheter.

Of the 204 cases operated upon in one stage 21 had chronic retention; there were 15 deaths, a mortality of 7.3%. Of the 21 patients with chronic retention 7 died, 4 from uræmia, giving a mortality in the chronic retention group of 33.3%. The 4 cases dying from uræmia had pre-operative blood urea figures of 20, 32, 36 and 43 mg. per 100 ml. respectively, but in each case the residual urine estimated at the time of operation was about two pints. 3 were good operative risks, and had they been drained first I think they would have lived and given a total mortality of about 5% instead of the actual figure of 6.2% for the whole series. Several of the patients with chronic retention who survived had an anxious post-operative course.

*The Avoidance of Sudden Decompression*

When there is hydronephrosis and hydro-ureter release of pressure affects the upper as well as the lower urinary tract. The renal blood vessels are adapted to an increased pressure and its sudden release may cause intrarenal hæmorrhage and tubular blocking.

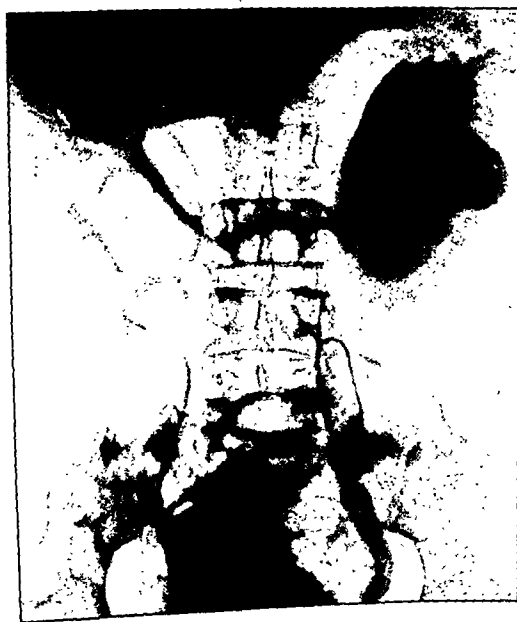


FIG. 1.—Pyelogram showing bilateral hydronephrosis and hydro-ureter in a case of chronic retention from enlarged prostate.

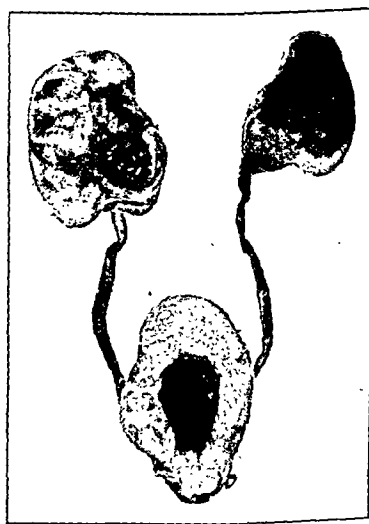


FIG. 2.—Autopsy specimen from same case as fig. 1. The dilated renal pelvis and ureters and the bladder are filled with blood clot. The bladder had been suddenly emptied by catheter.

A man of 69 had prostatic symptoms for six years and overflow incontinence for a month. He was catheterized and emptied completely of 35 oz. of clear urine. After a few days profuse hæmaturia started and he was again catheterized. On admission to hospital ten days after the first catheterization

he had a distended bladder and a blood urea of 186 mg. per 100 ml. Slow decompression through a suprapubic catheter with intravenous medication brought the blood urea down to 157 mg. but bleeding continued so copiously that I cystoscoped him. There was clot and active bleeding from each ureteric orifice and pyelography showed bilateral hydronephrosis and hydro-ureter (fig. 1). He died in uræmic coma eighteen days after catheterization with a blood urea of 205 mg. per 100 ml. At autopsy both renal pelvis and ureters and the bladder were found filled with blood clot (fig. 2).

I have seen other similar cases, particularly during the war.

#### *The Method of Drainage*

Any method used must comply with the principles of avoiding sudden decompression, infection and urethral trauma, and must not make the subsequent prostatectomy more difficult or hazardous.

*Urethral catheterization* may cause urethral trauma; it carries a high risk of infection and antibiotics may not be the complete answer. In 643 cases, (Rees, 1947) there were 18 deaths during gradual decompression by urethral catheter of which 9 were infective. If it could be foretold that it would not be required for more than two days it would be relatively safe but this is not always possible. Hey (1945) stresses the importance of infection.

*Urethrostomy*.—Sandrey (1949) claims advantages from the gravitational drainage. He reported a mortality of 8.6% in 58 poor-risk cases. I feel that the disadvantages of urethrostomy lie in the difficulties of nursing and of ambulation, and it still leaves the prostatic urethra exposed to catheter infection and trauma.

*Suprapubic cystostomy* as generally performed leaves a scarred abdomen for the second stage and the large tube often used leads to early infection and a leaking fistula with delay in healing after prostatectomy. The mortality is high, Rees (1947) reporting 30 deaths in 106 cases (28%) of which two-thirds were due to infection. In Australia, Howarth (1949) collected records of 1,000 consecutive prostatic cases with a 38% mortality from suprapubic cystostomy.

*Suprapubic catheterization*, the method I described in 1943, differs from cystostomy in that a small catheter (16F.) is used and, under a local anæsthetic, is inserted high on the abdominal wall. The joint is watertight and slow decompression can be carried out over a Kidd's U tube; this is completed in twelve hours after which the patient can be ambulant. It is possible to keep the urine sterile for from ten to fourteen days provided no washing out is allowed, and even if infection does enter it is confined to the bladder which can drain freely. If a long period of drainage is required a larger catheter can be substituted after two weeks and a leak-proof fistula can be guaranteed. The field for prostatectomy is unscarred and the fistula closes very quickly and, in fact, rarely leaks after the second stage, owing to the obliquity of the track (fig. 3). The disadvantage of the method is that it requires a special



FIG. 3.—Suprapubic catheterization in a case of chronic retention due to calculous prostatitis and stricture. The catheter enters high and is directed obliquely downwards and backwards into the bladder.

instrument and some common sense in using it as a stab method only when the bladder is properly distended. The same method can be used after exposing the bladder through a small high incision. In the past 5½ years I have used it as a first stage of prostatectomy or resection in 245 cases of prostatic obstruction; there were 14 deaths, a mortality of 5·7%, but in 3 of the cases it was merely used as palliative drainage in patients dying of heart failure or advanced carcinoma. If these are excluded the mortality is 4·4%.

*Suprapubic aspiration* finds its best use as an alternative to a catheter in acute retention when circumstances are unfavourable to asepsis. I have used it in chronic retention but a longer period of drainage is usually required than is afforded by the needle. The suprapubic catheter was designed to afford this period without unduly enlarging the opening and so increasing the risk of infection.

*Ureteral obstruction.*—A patient with lymphatic leukaemia had a grossly distended bladder, urea clearance was 24%, the blood urea rose to 208 mg. per 100 ml. and excretion pyelography showed no shadow up to one hour. He had a large prostate and cystoscopy showed an intravesical projection extending up to involve the ureteric orifice on each side. Nevertheless after suprapubic catheterization the blood urea fell in five days to 88 mg. per 100 ml. and to 48 mg. per 100 ml. in three weeks and I removed a prostate weighing 3½ oz. by the retropubic route; he had an uneventful convalescence under a streptomycin cover.

I am therefore not convinced that direct ureteral obstruction by the prostate is of major importance.

#### *The Atonic Bladder*

After the bladder has been overdistended for a considerable time it regains its normal tone slowly and sometimes not at all. Such a patient may come safely through a prostatectomy only to continue to have a large residual urine and to die after six months from uraemia. The value of prolonged suprapubic drainage before operation in such a case minimizes this risk; the alternative is to leave a suprapubic catheter for several weeks after operation at a time when the patient thinks he should be allowed to heal. Long pre-operative drainage is associated with bladder infection but resistance develops.

#### *Carcinoma of the Prostate*

When the prostate shows undoubted evidence of malignancy in a case of chronic retention the bladder will usually become gradually smaller under the influence of stilboestrol and artificial drainage can be avoided.

Finally I would like to quote one case of chronic retention where recovery occurred with a blood urea of more than 400 mg. per 100 ml. The man was 57 and was admitted medically for investigation of a supposed peptic ulcer. His bladder was found to be distended well above the umbilicus, he was drowsy and the blood urea was 420 mg. per 100 ml. and alkali reserve 36·5 c.c. After suprapubic catheterization and intravenous alkalis the blood urea fell to 38 mg. per 100 ml. after eight weeks and the alkali reserve was restored to normal. He came safely through a Harris prostatectomy; the suprapubic catheter was retained for twenty days after operation and the wound was dry the next day. He spent thirteen weeks in hospital, but he went out alive without the aid of penicillin or streptomycin.

#### REFERENCES

- HEY, W. H. (1945) *Brit. J. Surg.*, 33, 41.  
 HOWARTH, V. (1949) Personal communication.  
 REES, W. SKYRME (1947) *Brit. J. Urol.*, 19, 83.  
 RICHES, E. W. (1943) *Lancet* (ii), 128.  
 SANDREY, J. (1949) *Post-Grad. med. J.*, 25, 71.

**Mr. David Band (Edinburgh):** Let us turn for a moment to the physiological problem with which we are so often faced in chronic urinary retention. It is axiomatic that when there is an intravesical obstruction the effects on the kidneys above are those on function rather than on anatomical outline. The buffer effect of a hypertrophic bladder detrusor muscle for a long time prevents the accumulation of residual urine. But the very thickening of the bladder wall shortens the intervals of diastole, and frequency and straining finally give way to a mounting residual urine. Such urine has a low specific gravity, and the excretion of chloride and urea has diminished. Since the transitional epithelium of the bladder wall is entirely protective in function, the alteration in the urinary constituents is due to a depressed renal function.

It is the duty of the kidney to deliver to the tubules a watery glomerular filtrate which by their dual function of secretion and reabsorption leads to the production of urine. Thus water, urea, and electrolytes are excreted, and by the excretion of non-volatile acids the acid-base balance of the blood is maintained. The ability of the kidney in health to convert

urea to ammonia and thus further deal with any excess of acid, as well as to excrete most drugs, is another aspect of renal function apt to be overlooked in disease, when it would be most required.

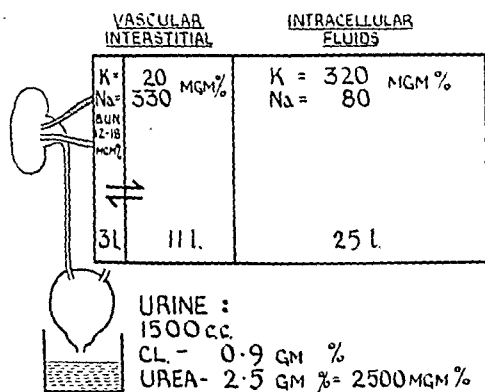


FIG. 1.—Shows a schematic representation of the body fluids in health. The vascular and interstitial fluids have a remarkably similar constitution. The interchange of constituents between the blood and interstitial fluid is brought about by the higher hydrostatic and osmotic pressure exerted by the blood so that a two-way interchange occurs through the capillary wall.

The customary biochemical estimations for blood nitrogen, blood chlorides, and the CO<sub>2</sub> combining power, when balanced against the qualitative and quantitative analysis of the urinary output, can usually provide the investigator with a fair idea of the impaired state of renal function. It is, however, difficult for him to estimate the amount of renal reserve he may be required to draw upon during the immediate period following the relief of the retention by whatever means—suprapubic catheterization, immediate prostatectomy, or simply perurethral catheterization. Intravenous urography is a valuable test in this respect, if the renal damage is believed to be minimal. It is probably unwise to carry out intravenous urography when the blood urea is above 50 mg. %.

There is another extremely important aspect in the management of chronic retention of urine which we cannot ignore. I refer to the age-group in which so often these patients occur and the accompanying cardiovascular lesions of a degenerative nature from which they suffer.

Edema and cyanosis indicate that the renal cells are still further embarrassed, and even if fluid exchanges through the capillary wall do occur, the ability of the kidney to excrete a concentrated urine has been lost.

Finally, alterations in the nature of the patient who has permitted a state of chronic urinary retention to continue for some time indicate a blunting of the finer attributes, owing to the uræmic state and possibly a boredom and apathy brought on by advancing years.

This clinical picture stresses the hazards of surgical intervention in chronic retention when defective renal secretion, altered blood chemistry, and a damaged cardiovascular system each requires individual consideration. Nevertheless, a patient who is ambulant and who will co-operate is always a likely candidate for the successful relief of urinary retention and the removal of the cause.

Undue emphasis has been placed on catheterization *per se* as being the cause of urinary infection in cases of chronic urinary retention. In a recent personal series I found that of 39 cases of chronic retention admitted to the wards, 10 had been catheterized prior to admission, and of these 5 had urinary infection. In 29 cases not catheterized prior to admission infection was already present in 7. This means that the percentage of cases of chronic retention with infection when first seen will always be considerable. When we take patients subjected to catheterization in the ordinary routine work of the ward, we find that in a series of 24 enuretic cases examined by the cystograph and catheterized, there was no occurrence of urinary infection after the examination.

In 35 cases of neurogenic bladder due to cerebrospinal disease or trauma, all suffered from a hypertonic bladder with residual urine and incontinence. 25 of these cases had urinary infection before they came under my observation and only 10 had sterile urine. In these cases an indwelling urethral catheter was employed together with tidal lavage and often followed by transurethral resection of the bladder neck. In the course of treatment I never found that the use of the indwelling catheter together with various antiseptic lotions in the tidal lavage apparatus would cure the urinary infection. It is true, however, that the use of various antibiotics and lotions could alter the nature of the organisms in the infected urine, and render a turbid urine clinically clear. I have come to the conclusion, accordingly,

that there is no harm in the indwelling urethral catheter, and with proper supervision its use should not introduce infection to the bladder.

In chronic urinary retention the bladder is either tonic when there is pain, or atonic when the distension has been insidious and the possibilities of renal deterioration are very real. Relief of retention and the restoration of a free excretion of urine may be achieved by suprapubic or perurethral catheterization. The catheter must be indwelling and the flow of urine unobstructed. So-called gradual decompression is unnecessary if the renal excretion is maintained. A knowledge of the blood chemistry and an analysis of the urine enable the clinician to give intravenous therapy of an appropriate nature. In many cases sodium chloride intravenously must be avoided unless there has been anorexia and vomiting. The use of isotonic sodium sulphate presumes the capacity of the damaged renal tubule to secrete sulphate. The value of isotonic dextrose is threefold. The blood volume is increased and the blood flow through the kidney improved. In addition the altered osmotic tension of the plasma leads to rapid dialysis between the circulating and tissue fluids, and urea and electrolytes are removed to the kidney to be excreted. The dextrose is quickly metabolized, but while in the plasma acts as a diuretic. Even in the presence of circulatory failure with oedema, intravenous dextrose may be employed in high concentration and in small quantities. 20 ml. of 50% dextrose may be injected intravenously at regular intervals over a critical period.

Antibiotic cover is now employed so universally in urinary surgery that sometimes these substances are employed without regard to the nature of the organism or its sensitivity to the antibiotic selected. Over-enthusiastic use of antibiotics would apparently lead to alterations in the nature of bacterial invaders, and similarly alterations in the sensitivity of different strains of microbe to antibiotic drugs. A close bacteriological check should be made in order to regulate the choice of antibiotic according to the organism present. The reaction of the urine may have an important bearing, e.g. in *B. proteus* and *B. pyocyaneus* infection. Lastly, I think that streptomycin should be held in reserve unless organisms or particular strains of organisms have been shown to be sensitive to streptomycin but unresponsive to other bacteriostatic agents.

Unskilful attempts at urethral catheterization cause pain, trauma, infection and shock. These are just the factors which lead to disaster in chronic retention with a disturbed renal balance. The development of peripheral circulatory failure is all that is required to produce fatal irreversible changes.

In the preliminary treatment of chronic urinary retention I would adhere to the employment of the indwelling urethral catheter. A strict asepsis is essential, and in the choice of catheter the quality of the rubber should receive consideration. The Foley self-retaining catheter or a Tiemann beaked catheter are most satisfactory, the one because of ease of retention, and the other on account of ease in negotiating the urethra. An indwelling catheter should receive the same attention as a surgical wound. Either a sealed retentive covering is employed, such as cellophane, or, conversely, a water-soluble dressing may be applied to the glans penis and changed at regular intervals. The cellophane has the advantage that a restless patient may alter the position of the penis and scrotum without disturbing the catheter. In the case of the water-soluble dressing, inspissation of secretion, which may cause retention of urethral secretion, can be avoided.

Having achieved free urinary drainage, the maintenance of renal secretion depends on the ability of the patient to resume a normal intake of fluid by mouth or intravenously. The value of intravenous dextrose has been mentioned above. A low blood-pressure may be of little significance provided the peripheral circulation is maintained.

While the balance of the urinary system is being re-established by the employment of the indwelling urethral catheter and the maintenance of an adequate fluid intake and output, the bacteriology of the urine and the urethral discharges should be watched. A considerable percentage of cases will be infected from the beginning, but, for the short period of employment of the urethral catheter, a proper use of antibiotics and attention to catheter hygiene should render so-called ascending infection a complication not now to be expected or feared.

The President said that the idea of the Discussion was to try to crystallize ideas on the treatment of chronic retention. Formerly it was the rule for a two-stage operation to be undertaken, but figures showed the relatively high mortality associated with suprapubic cystostomy. Five years ago Mr. Wilson Hey introduced his revolutionary theory of immediate prostatectomy with aseptic precautions, which captured the imagination, and many urologists had tried it out, some remaining strong supporters of that method, while others had abandoned it. There had been deaths from uræmia which were not met with commonly in other methods, and he agreed with Mr. Band and Mr. Riches that a preliminary period of



decompression was generally preferable. He had not used slow decompression for many years; anybody with an intimate knowledge of the bladder dynamics knew that there was no such thing as the decompression of the chronically distended bladder. One other point was that all agreed that any operation on the prostatic patient must be regarded as a major procedure; they could not forget such entities as subclinical uræmia and subclinical diabetes, which might reveal themselves only after operation; a few days' preliminary study could avert disaster.

Mr. Wilson Hey appeared to have retracted a little from his original standpoint in that he admitted that in 4% of cases he now employed a preliminary decompression.

The treatment of these cases was of great importance. In a personal series, out of 238 cases operated upon, 65 were afflicted with chronic retention. It was a matter of personal choice whether the bladder was emptied by the suprapubic catheter or by the indwelling urethral catheter; both called for some skill; they had to be carried out under aseptic precautions. A question raised largely by Lane is the problem of the tube tract in carrying out a stab cystostomy, as without an incision of the fascia, cellulitis was likely to occur without free drainage along the tract if the bladder were infected. It seemed better to use a tube passing loosely through the fascia. He was old-fashioned enough to employ a small No. 15 Ch. Tiemann catheter. If the patient was not considered to be fit at the end of a fortnight's catheter drainage, then a suprapubic tube was inserted. Only 3% of his cases required this.

Ureteric obstruction was very interesting. Mr. Wilson Hey claimed that the prostate caused this by direct pressure, but the obvious reply was that a high proportion of chronic retentions were due to a fibrous prostate which could scarcely compress the orifices with consequent ureteric dilatation; the large prostate could of course do this, and in fact did so. Kovarovicz of Prague had shown by intravenous urography on the operating table ureteric dilatation which subsided promptly on removal of the prostate, and recurred when the prostatic cavity was packed. The logical deduction was the danger of packing the prostatic cavity for any length of time. That work had been confirmed in France.

Then there were the ultimate functional results in these chronic retention cases to be considered. The atonic bladder did remain a problem. Recently Stock and Wells had written thus: "Two outstanding surgeons, Thompson in London, and Guyon in Paris, both considered that in the patient with chronic retention, the bladder had become atonic and lost its power to contract and that it would not regain this power even if the obstruction was removed. In some quarters this superstition persists to the present day!" That superstition still persisted in the Presidential Chair. He had no doubt that vesical atony could exist in the absence of any demonstrable obstruction. He had a patient who owned a public house. He opened at 6 and closed at 10.30; he was afraid to leave the bars during that time lest his assistants should help themselves to the whisky, and he consumed a vast quantity of beer with his customers. He appeared to have acquired a mega-bladder, and ultimately presented himself with marked difficulty in voiding, and a markedly distended bladder. Endoscopy revealed no apparent bladder neck obstruction. Cystography confirmed the presence of a bladder that held 2,000 c.c. without any discomfort. Hemi-cystectomy was carried out, and normal micturition with a good stream resulted.

He hoped that some of the subsequent speakers would dwell on the functional results in the atonic bladder. Some of these atonic bladders did not regain ability to empty completely after a properly conducted prostatectomy, and sometimes for this reason the urinary infection did not clear, and might even proceed to a uræmic death months later. He showed skiagrams of a case of chronic retention with markedly dilated upper tracts who underwent a most successful retropubic prostatectomy. The patient became symptom free, urine clear, ureters returned to normal size, but 8 oz. residual persisted.

Mr. H. P. Winsbury-White said that with many the question of whether or not the bladder should be decompressed was still undecided. Personally, he found that certain bladders with a large amount of chronic retention could quite safely be submitted to one-stage prostatectomy or resection of the bladder neck, provided one knew a good deal about the renal functions. Blood urea estimation was not enough. His practice was to have an intravenous urogram in all cases except those of very high blood urea, perhaps 200 mg. per 100 ml. or so, but in others it had been his practice to have intravenous urography as an excretion test of the kidneys. He would give details of the most recent gross case which he had had:

A man of 63 was admitted to hospital with his bladder half-way between his umbilicus and his sternum—there were 73 oz. of residual urine; the blood urea was 35 mg. per 100 ml.; the intravenous urogram showed excellent function of both kidneys; there was a mild degree of dilatation of both kidneys and ureters. He decided on these findings that this was a suitable case for a one-stage removal of the bladder-neck obstruction.

There having been no other pre-operative instrumentation, the patient was cystoscoped on the

table, as was his practice in such cases, and then he found there was a vesical diverticulum as well. This was considerable and he excised it extravesically; he did a diathermy excision of the bladder neck and the patient did not cause very much anxiety during convalescence.

He had dealt with many cases with marked chronic retention by one-stage prostatectomy and had not regretted it. It was important to use intravenous urography as a test of renal function. If the kidneys showed marked dilatation with the intravenous urogram then he would not do it.

As for decompression, in most cases it should take only twelve hours to decompress a bladder. One usually got the decompression done within that time but every now and then one had a patient whom it was difficult to decompress very quickly. He had a patient in mind who came in with his bladder up to his sternum; he tied in a catheter and decompressed him, 10 oz. every two hours, and it had no effect. It was important to note whether the patient had polyuria.

He did not believe that there was any need for the high mortality of suprapubic cystostomy. The mortality in 148 cases of his own, including those which went on to second-stage prostatectomy, was 6.7%. Results were very much a matter of technique. He used the minimum of operative interference, for example, the method which Mr. Riches employed, except that he always exposed the bladder and put in a prevesical drain. He thought that the last point was very important; moreover whenever he could he avoided indwelling catheter drainage. He attributed his low figures to these facts.

**Mr. D. Innes Williams:** *The atonic bladder.*—Through the great kindness of Mr. Ogier Ward, I have recently had an opportunity to study a short series of cases of chronic retention due to the atonic bladder, and I have also seen patients under the care of Mr. Barrington and Mr. Sandrey.

The term "atonic bladder" is usually inaccurate, for most of these bladders are really hypotonic—weak in relation to the normal resistance of the bladder neck and urethra, rather than completely without tone. It therefore follows that anything which lessens this resistance will improve the power of the bladder to empty itself.

All chronically distended bladders are more or less hypotonic. We are concerned only with those in which the tone is not rapidly recoverable. To be physiologically accurate, we should make a distinction between the sustained tonus contraction and the voiding contraction of the detrusor, but in clinical practice these are closely related and we mean by the atonic bladder one of large capacity and large residual, which fails to empty itself, even in the absence of obstruction. It is lax to palpation and is often difficult to feel at all, although it contains 20, 30 or 40 oz. The ureters and kidneys are characteristically unaffected by the enormous distension of the bladder and the blood urea remains normal as long as the urine remains uninfected. The outline of the apex of the bladder is dome-shaped; when emptied, the walls tend to fall together in folds, instead of contracting and at cystostomy the folds may be so prominent as to render inspection of the trigone difficult—though this phenomenon may also be due to œdema.

The patient with the atonic bladder is frequently in good general condition and may be aware that his abdomen has been distended for some time; he has usually found that straining is a help in passing water and some patients adopt the squatting position or use manual pressure. On introducing a catheter, with the patient lying down, the urine will only dribble out slowly and will not run at all if the end of the catheter is raised more than an inch or so above the level of the symphysis. Cystometry may be a help in following the progress of a case, but we have not thought it essential in establishing the diagnosis.

I have here attempted a rough clinical classification of the cases in this series: (a) Neurogenic atony; (b) exhaustion or over-distension atony; (c) primary detrusor atony; (d) combined rectal and vesical atony in the aged.

*Neurogenic atony* is a well-recognized condition, but I should like to make one point in connexion with the atony which results from diabetic neuritis. In this condition the urinary disorder, virtually indistinguishable from the tabetic bladder, may be the only evidence of the neurological lesion. There were 2 cases, a man and a woman, both known to have been diabetic for some years, in whom the vesical dysfunction was sufficiently characteristic to prompt the neurologist who saw them to make the diagnosis of diabetic neuritis in the absence of any other signs in the C.N.S. The man was greatly improved by perurethral resection of the bladder neck and it is interesting to notice that before the operation he suffered several hypoglycæmic attacks—because, owing to the enormous residual, the amount of sugar in the urine passed from the bladder bore very little relation to the amount in the urine being secreted by the kidneys and he was sometimes misled into supposing that

he required an increased dose of insulin when, in fact, a satisfactory balance already obtained.

I have called the second group *exhaustion atony*. When an obstruction is present, and the detrusor has hypertrophied in response to that obstruction, true atony of a permanent character is extremely rare, though a temporary lack of tone has been observed after one-stage closed prostatectomy and I believe that, in the chronically distended bladder, drainage may often be required for longer than the four or five days customary with the retropubic operation.

However, there have been a few cases in this series of long-standing bladder neck obstruction of the Marion type, in which a considerable residual has persisted after adequate removal of the obstruction and it seems that some degree of atony, perhaps an irreversible elongation of the fibres, might account for this.

Crabtree and Muellner (1948) advocate the removal of a large part of the bladder wall in these cases.

In one case in this group, a man of 73, who had been attending for many years for dilatation of a stricture and who was known to have a slight enlargement of the prostate, was found to have a residual of 26 oz. A cystogram (fig. 1) shows a diffuse bulging of the anterior wall of the bladder—



FIG. 1.

there is no sign of a neck to this sac—it is not a diverticulum. The bladder was difficult to palpate despite the residual and it caused him little inconvenience for two years, until last August 1948, when the urine became severely infected and he was admitted for prostatectomy. At operation, the prostate was small and fibrous and was removed only with difficulty; the bulging anterior wall of the bladder consisted of thick but flabby muscle, and, after a few days, it prolapsed through the cystostomy wound. At a second operation a large part of the bladder wall was cut away, and following a long period of catheter drainage he healed up and recovered the power to empty his bladder. This may be an example of exhaustion atony affecting only a part of the bladder wall.

Atony does not appear to affect those bladders in which there has been a comparatively rapid onset of obstruction due to large prostatic adenomata and if a residual persists after operation other factors, even apart from post-prostatectomy obstruction, are probably responsible. In one case infiltration of the bladder wall with inflammatory cells was the cause; in another marked lethargy due to cerebral arteriosclerosis seemed to render the patient insensitive to the filling bladder and inattentive to its emptying.

In some old men, with slight enlargement of the prostate and vesical distension, the bladder wall remains thin and smooth, the upper urinary tracts unaffected and the blood urea normal: these are the true cases of silent prostatism. It seems that if obstruction was ever a factor the detrusor never showed its normal response to obstruction, perhaps a senile failure of muscle is responsible. A typical case was an old man of 78 who had known that his bladder was distended for three years, but was not seriously inconvenienced by it, his general condition remained good and his urine uninfected. The prostate was a little en-

table, as was his practice in such cases, and then he found there was a vesical diverticulum as well. This was considerable and he excised it extravasically; he did a diathermy excision of the bladder neck and the patient did not cause very much anxiety during convalescence.

He had dealt with many cases with marked chronic retention by one-stage prostatectomy and had not regretted it. It was important to use intravenous urography as a test of renal function. If the kidneys showed marked dilatation with the intravenous urogram then he would not do it.

As for decompression, in most cases it should take only twelve hours to decompress a bladder. One usually got the decompression done within that time but every now and then one had a patient whom it was difficult to decompress very quickly. He had a patient in mind who came in with his bladder up to his sternum; he tied in a catheter and decompressed him, 10 oz. every two hours, and it had no effect. It was important to note whether the patient had polyuria.

He did not believe that there was any need for the high mortality of suprapubic cystostomy. The mortality in 148 cases of his own, including those which went on to second-stage prostatectomy, was 6·7%. Results were very much a matter of technique. He used the minimum of operative interference, for example, the method which Mr. Riches employed, except that he always exposed the bladder and put in a prevesical drain. He thought that the last point was very important; moreover whenever he could he avoided indwelling catheter drainage. He attributed his low figures to these facts.

**Mr. D. Innes Williams:** *The atonic bladder.*—Through the great kindness of Mr. Ogier Ward, I have recently had an opportunity to study a short series of cases of chronic retention due to the atonic bladder, and I have also seen patients under the care of Mr. Barrington and Mr. Sandrey.

The term "atonic bladder" is usually inaccurate, for most of these bladders are really hypotonic—weak in relation to the normal resistance of the bladder neck and urethra, rather than completely without tone. It therefore follows that anything which lessens this resistance will improve the power of the bladder to empty itself.

All chronically distended bladders are more or less hypotonic. We are concerned only with those in which the tone is not rapidly recoverable. To be physiologically accurate, we should make a distinction between the sustained tonus contraction and the voiding contraction of the detrusor, but in clinical practice these are closely related and we mean by the atonic bladder one of large capacity and large residual, which fails to empty itself, even in the absence of obstruction. It is lax to palpation and is often difficult to feel at all, although it contains 20, 30 or 40 oz. The ureters and kidneys are characteristically unaffected by the enormous distension of the bladder and the blood urea remains normal as long as the urine remains uninfected. The outline of the apex of the bladder is dome-shaped; when emptied, the walls tend to fall together in folds, instead of contracting and at cystostomy the folds may be so prominent as to render inspection of the trigone difficult—though this phenomenon may also be due to œdema.

The patient with the atonic bladder is frequently in good general condition and may be aware that his abdomen has been distended for some time; he has usually found that straining is a help in passing water and some patients adopt the squatting position or use manual pressure. On introducing a catheter, with the patient lying down, the urine will only dribble out slowly and will not run at all if the end of the catheter is raised more than an inch or so above the level of the symphysis. Cystometry may be a help in following the progress of a case, but we have not thought it essential in establishing the diagnosis.

I have here attempted a rough clinical classification of the cases in this series: (a) Neurogenic atony; (b) exhaustion or over-distension atony; (c) primary detrusor atony; (d) combined rectal and vesical atony in the aged.

*Neurogenic atony* is a well-recognized condition, but I should like to make one point in connexion with the atony which results from diabetic neuritis. In this condition the urinary disorder, virtually indistinguishable from the tabetic bladder, may be the only evidence of the neurological lesion. There were 2 cases, a man and a woman, both known to have been diabetic for some years, in whom the vesical dysfunction was sufficiently characteristic to prompt the neurologist who saw them to make the diagnosis of diabetic neuritis in the absence of any other signs in the C.N.S. The man was greatly improved by perurethral resection of the bladder neck and it is interesting to notice that before the operation he suffered several hypoglycæmic attacks—because, owing to the enormous residual, the amount of sugar in the urine passed from the bladder bore very little relation to the amount in the urine being secreted by the kidneys and he was sometimes misled into supposing that

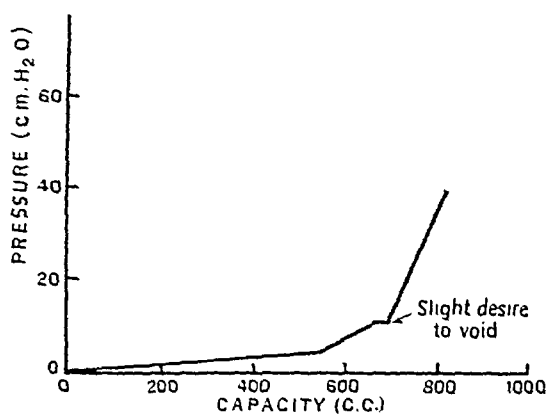


FIG. 3.—Primary atony of bladder. Cystometrogram after resection of bladder neck and three months' continuous drainage.

Dr. F. M. R. Walshe, could find no signs in the C.N.S. and C.S.F. examination revealed nothing. The bladder was trabeculated and the bladder neck slightly relaxed. He was taught to empty the bladder by squatting down and using manual pressure, and he managed very well for many years. During the war, however, he rejoined the Merchant Navy and visited the U.S.A. where a perurethral resection was performed. This procedure did not affect the atonic condition of his bladder, but did cause a stricture of the urethra. This stricture has now been satisfactorily dilated, his upper urinary tract has suffered no damage during the fourteen years for which he has been observed and he continues to empty his bladder by pressure.

As to diagnosis, I do not believe that the presence or absence of trabeculation is of great importance: even in cases where the bladder wall remains thin, some of the muscle bundles appear prominent, due perhaps more to wasting of the tissue between them than to their own hypertrophy.

There were 7 cases, including 2 women, in my fourth group in which vesical distension was accompanied by rectal atony: the bowel being filled with an enormous accumulation of faeces, despite a lax sphincter, through which leaked faecal mucus; in 2, the mass of faeces appeared to have precipitated acute retention. The prostate was either normal, slightly enlarged, or had been previously removed, and did not appear to be a significant factor in the retention. The cystometrogram (fig. 4) shows extreme atony in one of them

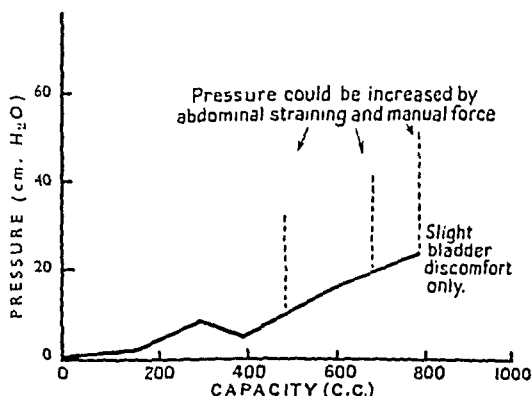


FIG. 4.—Combined rectal and vesical atony in the aged. Cystometrogram after fifteen days' drainage.

and the section shows fibrous tissue replacing almost all the muscle. These cases should easily be distinguished from the case of the enlarged prostate with uræmia, in whom rectal incontinence is not uncommon, but who normally recover continence as the blood urea

larged and was resected after a period of preliminary drainage; micturition was not resumed despite a second resection and it was noticed that the bladder showed very little power to return wash-out fluids and that it could not be felt even when it contained 25 oz. Permanent suprapubic drainage was instituted, at which time it was shown that the resection had been adequate, but that the bladder wall was very thin—histologically the muscle shows signs of degeneration. Not long afterwards the patient's general condition began to deteriorate, doubtless due to urinary sepsis, and he died some months later. In this type of case, if the true nature of the condition could be established clinically, it would be better to refrain from any instrumentation or treatment.

Atony accompanying urethral stricture has received very little attention in the literature, yet I have seen two cases in this series. Of course, residual urine is very rarely found in association with a stricture which is undergoing periodic dilatation to a reasonable calibre and when it does occur, it may well be due to a fibrosis of the prostate and bladder neck, resulting from the original disease or from the trauma of instrumentation. In one case in this series, a cystostomy was required because of the enormous residual; the bladder neck was normal, a straight X-ray shows the huge dome-shaped bladder and the cystometrogram (fig. 2), after two months' drainage, shows no return of tone. In another case, the patient

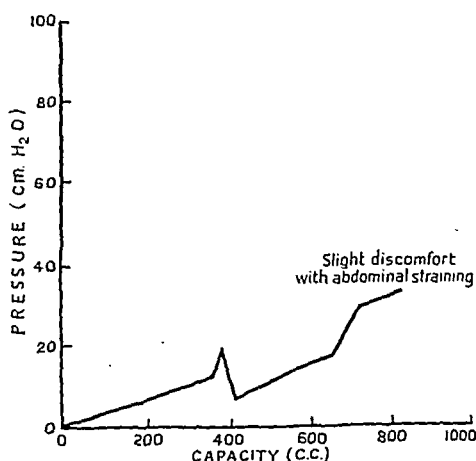


FIG. 2.—Atony associated with urethral stricture. Cystometrogram after two months' cystostomy drainage.

has a residual of 20–30 oz. despite a stricture which easily admits 25 Charrière instruments—and a recent operation for stones which had formed in a perineal pouch resulting from an old external urethrotomy, allowed palpation of the bladder neck, which was normally open and supple.

There were 4 patients in whom neither obstruction nor neurological lesions could be demonstrated and who have been labelled primary atony. In 2, both of them old men, although there was no evidence of bladder neck obstruction as seen through the foroblique telescope, the retrograde view did reveal a collar around the internal meatus, more marked anteriorly. Resection was undertaken without improvement in either case. One man had a permanent cystostomy—the bladder wall was thin but histologically normal; the other has worn an indwelling Foley catheter for four months, without recovery of tone—as shown by cystometrogram (see fig. 3). Braasch and Thompson (1934) regard this collar seen with the retrograde telescope as evidence of spasm or cicatrization of the internal sphincter and as a definite obstruction, but even if this is true, there can be no doubt that, as in the case of silent prostatism, the detrusor has failed to show its normal response to obstruction and the idea of senile muscle failure again suggests itself. It is possible that the collar around the internal meatus is merely the slight normal elevation rendered more obvious by the atrophy of the expulsive musculature.

However, not all cases of primary atony occur in old men.

The following case of Mr. Sandrey's first came up in 1935 at the age of 42. He then had a history of a few months difficulty of micturition which necessitated straining; the bladder was revealed by percussion to be distended above the umbilicus and contained 60 oz. residual. The prostate was normal to rectal examination and cystoscopy, the blood urea was 25 mg.%, I.V.P. normal. The neurologist,

period of decompression went on for forty-eight hours. He surrounded the penis with sulphamide powder and wrapped it in cellophane and this prevented other organisms gaining access. Under the principle of Trueta such organisms as were present killed themselves. The whole was sealed up by waterproof strapping, the catheter was not changed very often and in a certain proportion the meatus was found to be sterile. The patients were given a blood transfusion, if necessary, which improved the blood supply to the kidneys. They were given plenty to drink and he believed that they needed sodium chloride.

**Mr. G. A. Bagot Walters:** It has been a very great surprise to me to-day to hear Mr. Wilson Hey talk about slow decompression. It is now some years since I was first privileged to see him at work, and from that time I adopted his principles to a large extent and my experience now covers 276 cases of benign hypertrophy. Presumably the reason this discussion has been confined to *chronic* retention is that nearly everyone is now agreed that immediate prostatectomy is the treatment of election for *acute* prostatic retention: my own experience certainly bears this out. As shown in Table I the operation rate was 95% and the cases of acute retention gave a mortality rate of 3.9% which is not unreasonable, more

TABLE I.  
BENIGN PROSTATIC HYPERTROPHY AND RETENTION OF URINE  
276 cases : 262 submitted to radical operation. 95%

|                                                               | No. of cases | No. of deaths | Mortality rate |
|---------------------------------------------------------------|--------------|---------------|----------------|
| Suprapubic prostatectomy (Hey or Millin; 2 Freyer; 1-2 stage) | 220          | 15            | 6.5%           |
| Perurethral prostatectomy (Punch)                             | 42           | 2             |                |
| Permanent suprapubic cystostomy                               | 7            | 1             | 14.3%          |
| No operation                                                  | 7            | 6             | 85.7%          |
| Cases of acute retention                                      | 127          | 5             | 3.9%           |
| Cases of chronic retention                                    | 50           | 6             | 12.0%          |
| Cases of prostatic syndrome                                   | 85           | 6             | 7.0%           |

particularly as two of the deaths occurred early in the series where preliminary treatment was by indwelling catheter for some days; one on account of cardiac failure (aged 76) and one who also had pneumonia on admission (aged 73).

My cases of true chronic retention, by which I mean a distended bladder with some overflow incontinence, number exactly 50 and there have been 6 deaths: blood ureas were nearly all over 80 mg. %, the highest being 266. This patient was doing reasonably well till on the nineteenth post-operative day we gave him a blood transfusion to expedite his recovery and he died from transfusion reaction. Admittedly the mortality rate of 12% is much too high but I would like to emphasize that the hospital at which I do most of my work admits *all* cases, and the senile and bad-risk patients cannot be sent to an "Institution" as happens in some areas. In no case could I attribute death particularly to sudden decompression and there was no evidence of renal hæmorrhages such as have been described.

Further support for sudden decompression has come in recent times from Hryntsckak of Vienna who, writing in the March Number of the *Journal of Urology* this year, concludes after sixteen years' experience of it that: "... sudden and complete decompression of the distended bladder can be carried out without danger—and has great advantages over the old method of slow and gradual decompression." Also Homb of Oslo in *Acta Chirurgica Scandinavica* (1948) writes: "58 patients with great chronic retention of urine were treated by complete emptying of the bladder on admission. From the experience of this material it seems that rapid decompression of the chronic distended bladder is not dangerous." It is evident, therefore, that sudden decompression has gained considerable ground and that soon no one will bother with gradual emptying. It seems to me that Mr. Riches' good results are due to his excellent asepsis rather than to taking twelve hours to empty the bladder.

This still leaves unsolved the problem of when prostatectomy should take place. Although I am convinced that immediate prostatectomy is the procedure of election for the majority of cases, I am now not doing this quite so frequently for the chronic distended bladder, and feel there is still a useful field for two-stage operations in selected cases. For example, in some cases of chronic over-distension the bladder is atonic and if the catheter is taken out on the fourth to sixth day the patient is not able to empty his bladder completely. This means that a further period of drainage is necessary so that we lose one of the most important advantages of immediate prostatectomy, namely a short period of catheter drainage—as it is this that lessens the danger of infection, the chief cause of mortality.

falls. It is natural to suggest a neurological cause for the atony of both viscera and Dr. George Riddoch, who saw one of the cases, thought there might be an arteriosclerotic lesion of the cauda equina; but no other neurological signs have been found in any of the cases and we have no information regarding the central nervous pathology. All the patients were well advanced in years and as in the previous groups, a senile muscle failure might be the explanation.

Summing up, the atonic bladder is rare and often diagnosed only after the failure of treatment. If we find a considerably distended bladder, which is not tense to palpation and in which overflow incontinence has preceded upper urinary tract damage, atony should be carefully considered. Where the prostate is definitely enlarged, it is almost certain that relief of obstruction and drainage will lead to recovery of the bladder tone; where the prostate is only a doubtfully obstructing factor, greater caution is required and in the very old it may be well to avoid instrumentation altogether.

#### REFERENCES

- CRABTREE, E. G., and MUELLNER, S. R. (1948) *J. Urol.*, 60, 593.  
BRAASCH, W. F., and THOMPSON, G. T. (1934) *Trans. Amer. Ass. Gen.-urin. Surg.*, 27, 99.

Professor Charles Wells said that in Liverpool they had been very interested in Mr. Wilson Hey's work for a long time and had set out to study in detail the changes in renal function in a series of cases admitted with acute retention. The hard work of this investigation had been done by Mr. Marcus, a Research Fellow in the Department, to whom the others were greatly indebted.

Professor Wells then briefly described a short series of cases in which immediate prostatectomy had been done as an emergency operation in spite of grossly diminished renal function. In all these cases, primary hæmostasis had been secured and the bladder closed, and in every case a very considerable improvement in renal function was demonstrated. This invariably began immediately after operation and sometimes its progress was extremely rapid.

He thought that an important contra-indication to operation was found in the patient who was unlikely to co-operate, whether from senility or uræmia, or any other cause. He regarded ambulation as an important feature in convalescence as it combated the ascent of infection to the kidney. If pyelonephritis did occur streptomycin should be used and might very well reverse the progress of the illness within a few hours.

The presence of a diverticulum was a point in favour of early operation through a clean field.

In the experience of the Surgical Unit in Liverpool intravenous pyelography was not unsafe in patients with high blood urea.

Finally, Professor Wells pointed out the difficulty in comparing groups of figures based on different criteria. Those who practised the immediate operation based their figures on total admissions, whereas those who practised drainage considered only patients who came finally to prostatectomy, in compiling statistics.

Mr. H. Donovan said that the previous speakers seemed to hold almost diametrically opposite views as to the significance of blood urea as a criterion of danger when operating on the prostate, and their views also substantially differed as to the danger of passing a catheter and emptying the bladder.

He was very interested to hear Mr. Band draw attention to the outstanding importance of the function of the renal tubule, and hoped that he would be able to adduce evidence by a detailed study of electrolytic excretion and retention to support his views that the renal tubule was failing. It seemed likely that the retention of urea in the body would cause the sodium chloride to be thrust out in an effort to maintain iso-osmosis, and then when the bladder was drained and the urea began to escape freely, there might be a consequent deficiency in sodium chloride.

The speaker went on to say that he was disappointed that no one had paid any attention to the study of the blood in these cases. It was his opinion that one could probably pick out the patients who were in danger of renal failure by means of the blood-count, for it was certain that those patients who were severely anæmic with blood-counts in the region of 3 million had been severely damaged by back pressure and were a most dangerous group.

In the case of patients such as these, he passed a catheter and decompressed gradually; he drew away 10 oz. and put in 1 oz. oxycyanide of mercury, which was an antiseptic. The



He thought that slow decompression was only permissible when both penicillin and streptomycin were used prophylactically.

Mr. Riches and he were not talking about quite the same group of patients. He himself was discussing the Group IV patients, on whom most surgeons would do permanent suprapubic cystostomies and on whom Mr. Pocock would not operate at all. In none of his own aseptic sudden decompressions had any blood been found in the ureters or the kidneys at the post-mortem examination. Intra-renal and intra-ureteric hæmorrhage will often occur in the presence of prolonged septic decompression.

He agreed entirely with Mr. Donovan and although the glucose-insulin-adrenaline drip was used most commonly, after estimation of the chlorides in the urine a normal saline drip was often used. Blood transfusions, whilst being necessary in those rare cases where blood loss was great, were dangerous in old people.

Daily catheterization over a very long period would usually improve or cure the atonic bladder after prostatectomy; and it seemed no more reasonable to resect a portion of the atonic bladder than the atonic stomach. He confirmed Mr. Band's statement that 25% or 50% solutions of glucose were at times invaluable in uræmia. He had discovered quite accidentally, whilst administering insulin and glucose in uræmia in such proportions as to cause hypoglycæmic coma, that after resuscitating with 50% glucose the uræmia had diminished enormously.

As regards spinal anaesthesia—so essential in the presence of high uræmia if further toxæmia was to be avoided—there was something wrong with Mr. Maitland's description of spinal calamities. He had never seen anything more than temporary saddle-shaped anaesthesia, retention or incontinence, and these not for many years. He always gave a minimum dose (1.4 c.c. of heavy percaine), did extensive barbotage, never allowed anaesthesia to go above the symphysis or analgesia above a point two-thirds of the way from the symphysis to the umbilicus. The patient should always be able to move his feet and have a flicker in the rectus femoris. In a patient suffering from spinal anaesthesia shock, there is a serious fall of blood-pressure on the table and perhaps irreversibility of that fall; he might not be mentally co-operative at any time afterwards; the resultant renal shock was such that the urinary output on the following day might go down to a few ounces instead of being well over fifty; the blood urea might rise instead of falling; and the patient was certainly more liable to thrombosis, both cerebral and pulmonary, during the subsequent fortnight. After prostatectomy the mental outlook was the most important factor and the cardiovascular the next.

Ureteric obstruction could be caused by the small fibrosed prostate, and indeed in one case quoted in which a ureteric catheter could not be passed at all, the prostate was small and fibrosed.

Mr. E. W. Riches, also in reply, said that he had not found any trouble from cellulitis of the tube track. It was an advantage to do without a prevesical drain because it left the tissues unscarred for the next stage. By making the catheter act as the cannula there was such a tight fit that ultimately a good track was formed.

Certain bladders would never regain their normal tone. He remembered that six years ago when he first described the suprapubic catheter (1943) he had a patient whose bladder held five pints after five years of prostatic obstruction. Two years after prostatectomy it still held two pints, and each night the patient removed 15 oz. of residual urine by means of a catheter.

He had been averse to using intravenous pyelography when the blood urea was over 100 mg. per 100 ml.; so often one saw nothing at all because of the poor renal function. He agreed that it gave more information about this type of case than any other single investigation and was prepared after hearing Mr. Winsbury-White and Professor Wells to use it more often, but Mr. Milward's remarks were a salutary warning. He had seen one death due to intravenous pyelography many years ago and it discouraged him from using it; one must exercise caution about doing an intravenous pyelogram in a case of chronic retention.

Mr. Williams had mentioned diabetic neuritis; *tabes diabetica* might mimic prostatic obstruction, but in one such suspected case the dysuria proved to be due to a cerebral tumour. From the other point of view, a patient with sciatica, thought to be due to carcinoma of the prostate, proved to have diabetic peripheral neuritis which disappeared when his diabetes was treated.

The method of bladder drainage was not so important now that antibiotics were available but he was still not going back to his temporary habit of doing a so-called "immediate" prostatectomy in cases of chronic retention. To drain the bladder first made for safety.

Certain other cases present a poor operative risk on account of chest or cardiac complications and there is quite a large group of patients suffering from hypertension who improve very much with preliminary drainage. For example, Mr. F., aged 78, was admitted with chronic retention and a B.P. of 240/120. His general condition was quite good and blood urea only 60 mg. % but he was strange in manner and confused mentally: following catheterization he became very restless and unco-operative. He was seen by a physician who diagnosed hypertensive encephalopathy. I performed a suprapubic cystostomy and now, three months later, his B.P. is down to 190/100 and his mental condition about normal. He will soon have a retropubic prostatectomy which will, I believe, be successful. I confess that two years ago I would have done an immediate prostatectomy with almost certainly a fatal result.

## REFERENCES

- HOMB, A. (1948) *Act. Chir. Scand.*, 96, 307.  
HRYNTSCHAK, T. (1949) *J. Urol.*, 61, 548.

Mr. A. I. L. Maitland congratulated Mr. Williams on his paper which had dealt with an aspect of the subject on which he would like to relate a recent personal experience and also to ask Mr. Wilson Hey a question related to his routine use of spinal anaesthesia.

A patient he had seen two weeks ago was found to have atonic retention due to a typical neurological bladder occurring in the course of an acute polyneuritis. Six months earlier a similar case was seen with no other neurological lesion, who was treated by suprapubic drainage with recovery of function which is by now almost complete. This suggests that the lesion may have been an acute neuritis affecting the bladder alone.

In the last 60 cases in which full investigation by cystoscopy and cystometry had disclosed neurological disturbances of the bladder 6 had previously had one or more spinal anaesthetics, in 5 of these the spinal anaesthetics had been given for general surgical procedures; in the sixth, a fit man of over 80, complete incontinence with a large flaccid bladder had followed its use for a major urological proceeding.

In the clinic in which he worked spinal anaesthesia, apart from 0.3 c.c. 20% planocaine, is not often used and he therefore had no knowledge of the proportion of the total number of spinal anaesthetics which this series represented. 6 out of 60 does represent a high proportion of the cases in which there is no visible sign of bladder neck obstruction or any other evidence of neurological disease.

He would therefore like to ask Mr. Wilson Hey how often vesical dysfunction or incontinence occurred when spinal anaesthesia was the routine method in use?

Mr. F. J. Milward said that when he was a student patients were killed when the bladder was emptied suddenly, and now it seemed to be done with impunity; was the explanation that now they had some degree of control over infection?

He thought Mr. Riches' case of the old gentleman who was catheterized and who did not start to bleed until five days later, just at the time when he might have been developing an infection in the urinary tract, was instructive, and it supported Mr. Wilson Hey's view of the cause of bleeding in these cases. He (Mr. Milward) had done a certain number of immediate prostatectomies, or prostatectomies without preliminary drainage, in the chronic retention class, on patients who had blood ureas between 100 and 280 mg. per 100 ml. Out of 15 such cases there were 2 deaths.

These cases needed endless watching, particularly with regard to fluid balance, and if anything went wrong the surgeon was in trouble. It only needed the catheter to become blocked and a sepsis went by the board when one started washing out. He thought equally good results could be obtained by certain preliminary methods of drainage, and he would commend Mr. Riches' apparatus; it was safe, it could be kept far more aseptic than a urethral catheter and it saved a good deal of worry.

As to the dangers of intravenous pyelography, he had a case which died on the table following an injection of uroselectan B: the patient was a young man with severe septic pyelonephritis following a traumatic stricture which had occurred in the Army.

Mr. John A. Pocock thought there was a group of patients who should not be operated on. A patient would attend hospital who was not incontinent, had a little frequency, but on clinical examination the bladder was enlarged up to the umbilicus. He considered there was a case for leaving certain of these people alone.

Mr. Wilson Hey, in reply, said that 98% of his prostatectomies were done at one stage, and he was certain that the two-stage operation was decreasing amongst surgeons as a whole.

## Section of Proctology

President—C. NAUNTON MORGAN, F.R.C.S.

[May 11, 1949]

### DISCUSSION ON PROLAPSE OF THE RECTUM

**Mr. A. Dickson Wright:** Rectal prolapse is a humiliating complaint, whether to the parents of the infant sufferer, generally a boy, or to the aged, generally a lady, whose closing days are rendered dirty and degraded by this condition. It is hard to think of a complaint more calculated to bring one's grey hairs with sorrow and relief to the grave.

The adult sufferers generally retire from all contacts with the outer world and live the life of social outcasts, and the opportunity for the surgeon to help them is heaven-sent, provided a good method of treatment is employed.

The disease can be classified as follows :

- (1) Simple rectal prolapse of the mucous membrane as a ring with or without associated hæmorrhoids, a weak sphincter being mostly but not always present.
- (2) Complete prolapse when the rectum turns inside out and by pulling down a portion of the peritoneal cavity in front proves itself to be a sliding hernia. This complete prolapse can be chronic and slowly developing and associated with a patulous sphincter, or acute and rapid with a tight sphincter and gangrene or near gangrene of the extruded portion.
- (3) Intussusception of the sigmoid starting just above the recto-sigmoid junction. In course of time this turns the rectum inside out and is indistinguishable from the last form.
- (4) Post-operative prolapse following operations on the rectum such as Whitehead's operation, pull-through operations of the Hochenegg and Roux type for cancer and accidental division of the sphincters in fistula operations.

Its occurrence in children probably derives from bad habits of defæcation and Saturday purgation combined with the infantile anatomy of the pelvis. In the decline of life it is part of the general herniating process manifesting itself at the openings of the abdominal cavity provided for the œsophagus, genital cords, femoral vessels

The ease of convalescence had to be considered also. These cases were a serious risk and anything which could minimize the risk should be done. Drainage should be continued until the blood urea had stabilized.

With the great improvement in modern intravenous anæsthetics he had given up using spinal anæsthetics altogether. One got the necessary relaxation safely without them. One should ask oneself the question, "If I had to have this done would I have a spinal anæsthetic" and the answer was "No".

#### REFERENCE

RICHES, E. W. (1943) *Brit. J. Surg.*, 31, 135.

Mr. Band, also in reply, said that it would be wrong to limit the intravenous therapy of the chronic retention patient to glucose only—he might require salt—but if he had been taking nourishment up to the time of admission then possibly glucose alone was the safest method of stimulating secretion and maintaining the blood flow through the kidney. One had seen so many tragedies from the over-use of intravenous chloride that one had swung a little away from it.

With regard to spinal anæsthesia in the retropubic operation where hæmostasis was secured by the use of sutures in the capsule, one could afford to have a low blood-pressure throughout the operation and when the subsequent rise came there would not be any post-operative bleeding. On the other hand, he would think that in the Wilson Hey operation it was important to deal with the vessels at each stage of the operation and secure hæmostasis while the blood-pressure remained at a reasonable level.

The President said it was interesting to see how renal function tests, elaborate as they had become, were being relied upon less and less, more stress being laid upon clinical assessment—the patient's tongue, ability to co-operate, &c. Tests were of course useful, and urograms and biochemical tests should still be done, but ultimately the decision as to when to operate was a matter of clinical judgment.

- (1) The excision of the pile area in cases in which the prolapse is simply mucous membrane.
- (2) The anal tightening operation of Thiersch for lesser degrees of true prolapse.
- (3) The rectosigmoidectomy operation of Miles.
- (4) The ligature method over a rubber tube for strangulated cases.
- (5) The pelvic obliterating operation of Moschowitz.

The Thiersch operation seems to be gaining rapidly in favour, not only for the medium cases for which it was first suggested, but for the severe cases. I have now had four cases of simultaneous procidentia of the uterus and rectum. The condition of these aged sufferers was indeed pathetic, but the simple introduction of a figure of eight silver wire with the loops encircling the anal and vaginal orifices with wires crossing the perineum produced a satisfactory result in a most simple way and allowed them to totter much more comfortably towards the grave. I have since used the single vaginal circle of wire for uterine prolapse alone in the aged with a most agreeable result.

The aseptic introduction of these wires is greatly helped with the hollow needles shown (fig. 1) and the operation can be carried out without any jerking or trauma.

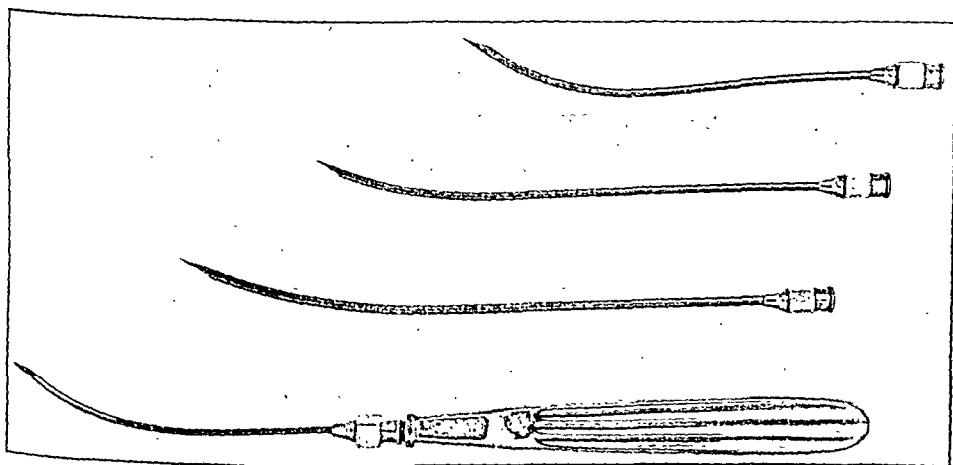


FIG. 1.—Sheehan's curved hollow needles for introduction of silver wire for procidentia operations.

I have endeavoured also to weld the wire together by sparking the diathermy current across at the first double turn of the knot in the wire. The use of a double knot or twisted ends is more likely to lead to extrusion of the wire by ulceration.

Following these operations, the patient must be warned against impaction and told about the existence of the wire so that she can restrain the ardour of any new doctor called in who might feel that the anus required dilatation.

**Mr. E. S. R. Hughes:** In seventeen years, from 1931 to 1947 inclusive, 426 cases of prolapse of the rectum attended St. Mark's Hospital. Of these, 231 were complete and the remainder partial or uncertain. This present investigation has been concerned only with the completely prolapsed rectum. There were 16 children, but their treatment does not present the difficulties found in the adult, and they were omitted from further study.

and rectum and uterus. Certain conditions predispose to rectal prolapse; the most common is vesical calculus and when this is dealt with the prolapse disappears immediately as a rule. Stricture of the urethra, phimosis and, to a lesser degree, prostatic obstruction also contribute to its development. Diarrhœa, especially when due to famine, is a possible cause and I believe it was observed in Belsen camp. The disease of lipodystrophia also leads to the condition from loss of perineal fat.

Anal coitus is also mentioned as a cause and perineal damage from childbirth sometimes initiates the condition. Heredity may predispose, as Ottenberg records a large series of cases in a small intermarrying Jewish community in East Prussia. From the same region the disease is also reported in a peculiar sect who indulge in rectal strainings with the rectum empty as one of their religious rites. From the same queerly behaved region was reported the artificial production of the condition in draft-avoiding recruits by repeatedly placing a sponge in the rectum with a string attached and then extracting the same by a sharp tug on the string.

In regard to the treatment, there has been a hard struggle with the problem and the large number of procedures discovered would indicate a vast number of disappointed patients and surgeons. I have been able to discover more than fifty different procedures recommended for this condition, many of them carrying quite a fair mortality rate. Thirty-six methods that have been extensively employed are as follows :

- (1) In infancy by altering habits and strapping buttocks together.
- (2) Thermo-cautery in streaks (Lundh).
- (3) Cautery with fuming nitric acid.
- (4) Excision of strips of mucosa with cautery (Hartmann).
- (5) Diathermy in streaks.
- (6) Diathermy of whole of prolapsed mucosa (Hey).
- (7) Submucous injections of carbolic acid in oil (5%).
- (8) Submucous injections of paraffin wax (Gersuny).
- (9) Submucous injections of ergot (Langenbeck).
- (10) Submucous injections of quinine and urea (Bensaude).
- (11) Submucous injections of glycerin and tannin.
- (12) Submucous injections of alcohol (d'Espine).
- (13) Peri- and retro-rectal injections of alcohol (Lorin Epstein).
- (14) Submucous injections of hydrochloric acid (Hanes).
- (15) Submucous injections of cow's or goat's milk (Schotter).
- (16) Encirclement of anus with silver wire (Thiersch).
- (17) Encirclement of anus with silk thread (Platt).
- (18) Encirclement of anus with rubber strand (Delbet).
- (19) Encirclement of anus with stout tube of rubber (Matte).
- (20) Encirclement of anus with tendon or fascia lata.
- (21) Encirclement of anus with hernial sac.
- (22) Encirclement of anus with strip of gluteus maximus.
- (23) Encirclement of anus and vagina with figure of eight of 20 S.W.G. silver wire (Dickson Wright).
- (24) Rectopexy to face of sacrum by suture (Gerard Marchant).
- (25) Rectopexy to face of sacrum by gauze packing (Sich and Lockhart-Mummery).
- (26) Colopexy to anterior abdominal wall (Ball and Radgiewsky).
- (27) Colopexy to iliac fossa (Quenu).
- (28) Colopexy combined with resection of sigmoid loop (v. Eiselsberg and Ludloff).
- (29) Obliteration of recto-vesical or recto-uterine pouch with silk purse-string sutures (Moschowitz).
- (30) Amputation of irreducible prolapse by rubber ligature over drainage tube.
- (31) Recto-sigmoidectomy (Mickulicz and Miles).
- (32) Resection of anal mucosa (Lenorme).
- (33) Resection of strips of anal mucosa (Duret).
- (34) Plastic operation on the sphincters and rectum via the perineum.
- (35) Repair of pelvic floor by suturing levatores ani across the mid-line in front of the rectum by perineal route (Schwartz).
- (36) Repair of pelvic floor by suturing levatores ani across the mid-line in front of the rectum by abdominal route (Roscoe Graham).

It is impossible to say what is happening in various parts of the world at the present moment, but it would seem that the main treatments used here are :

patients who underwent surgical treatment had a total of 304 operations performed on them at St. Mark's Hospital and elsewhere.

The majority of operations have been conducted through the perineum; some have been abdominal, and a few patients have had two-stage procedures, an abdominal operation followed by perineal, or vice versa.

(1) *Lockhart-Mummery's posterior proctopexy*.—Posterior proctopexy, wherein the rectum was fixed to the sacrum by scar tissue, was given a thorough trial by Lockhart-Mummery, one of St. Mark's most eminent surgeons. There were no successes, and the recurrences took place, as a rule, shortly after operation (Table III).

TABLE III.—ST. MARK'S HOSPITAL

Lockhart-Mummery's posterior proctopexy { 33 cases (30 traced) }  $\frac{1 \text{ died}}{29 \text{ recurred}}$

(2) *McCann's operation*.—In this operation the space in front of the rectum is exposed through an incision in the posterior vaginal wall, and the two levator muscles and neighbouring pelvic fascia are sutured. Only three such procedures were carried out, but none was effective.

(3) *Rectosigmoidectomy*.—In a rectosigmoidectomy operation, the prolapse is amputated, the peritoneum opened, the redundant colon is withdrawn until it is taut, and it is then sutured to the mucosa of the anal canal.

TABLE IV.—RECTOSIGMOIDECTOMY 150 CASES, 108 TRACED (NO DEATHS)

| Recurrence 65 (60%)       |     |  | No recurrence 43 (40%) |    |                               |
|---------------------------|-----|--|------------------------|----|-------------------------------|
| Continent .. ..           | 6   |  | Continent .. ..        | 15 | Stricture:                    |
| Incontinent .. ..         | 39  |  | Incontinent .. ..      | 21 | Obstruction 3                 |
| Severe .. ..              | 24  |  | Severe .. ..           | 8  | Acute 2 (at seven and         |
| Moderate .. ..            | 7   |  | Moderate .. ..         | 7  | eight years)                  |
| Mild .. ..                | 8   |  | Mild .. ..             | 6  | Chronic 1 (six years)         |
| (Not known whether conti- |     |  | (Not known whether     |    | Chronic ulcerative colitis 1  |
| nent or incontinent ..    | 20) |  | continent or inconti-  | 3) | (Colectomy at fourteen years) |

There were no operative deaths in 150 cases (Table IV). It was possible to trace the results of 108 operations; 65 (60%) recurred and at the time of the follow-up, 43 (40%) had not recurred. In 92 instances the results were confirmed by examination, and in 16 it was necessary to depend on a written answer to a questionnaire. Most of those who had recurred were incontinent to a more or less severe degree. It has been found that the patients with an untreated prolapse are frequently continent, and hence rectosigmoidectomy has not only been unsuccessful in curing the prolapse but has made the patient incontinent, and often severely so. Of the 43 which had not recurred (and 20 have been followed for three years or less), 21 were incontinent, 8 very badly, after the operation. Experience has shown that some of the more moderate and milder degrees of incontinence may improve with the passage of time. 4 patients developed severe strictures some time after operation; in 1 chronic ulcerative colitis supervened and a colectomy was necessary fourteen years after operation; in the other 3 emergency treatment was subsequently required for intestinal obstruction after six, seven, and eight years respectively.

TABLE V.—THE UNSUCCESSFUL RECTOSIGMOIDECTOMY

- (1) No relation to age, duration of prolapse, or sex.
- (2) The average length of bowel excised was 8–14 inches.

| Recurrence                              |                                     |
|-----------------------------------------|-------------------------------------|
| 23% in first year                       | 9% in third year                    |
| 18% in second year                      | 6% in fourth, fifth and sixth years |
| Some recurred more than ten years later |                                     |

A very large series of patients with complete prolapse of the rectum such as this is most unusual, and attention was drawn to certain clinical features.

(1) *Sex*.—Complete prolapse of the rectum occurs much more frequently in females; for every male patient there are 5 or 6 females, i.e. 85% females, 15% males.

(2) *Age*.—In males, the highest incidence is in the 2nd and 3rd decades, although the prolapse may appear at any age. In females, the maximum incidence is later in life (fig. 1).

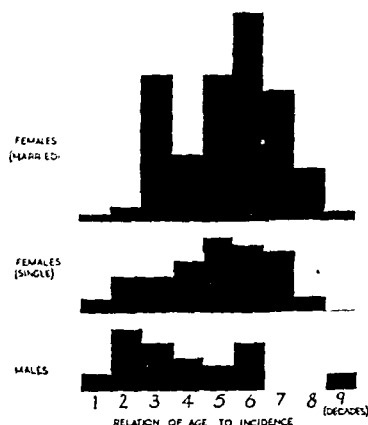


FIG. 1

(3) *Parturition*.—There is a relatively high incidence in females who have never been pregnant. Of 183 women, 120 were married and of these 10 had no pregnancy. Of 63 single, 1 had been pregnant. Occasional patients have attributed the prolapse to a confinement and have believed the prolapse aggravated by subsequent pregnancies (Table I).

TABLE I

| Age at onset | Date of onset | Date of pregnancies |      |      |      |      |  |
|--------------|---------------|---------------------|------|------|------|------|--|
| 29           | 1933          | 1931                | 1932 |      |      |      |  |
| 30           | 1922          | 1912                | 1914 | 1916 | 1921 | 1927 |  |
| 31           | 1928          | 1922                | 1932 | 1934 |      |      |  |
| 28           | 1900          | 1897                | 1899 | 1901 | 1906 | 1908 |  |
| 42           | 1924          | 1918                | 1920 | 1924 |      |      |  |
| 27           | 1908          | 1901                | 1906 |      |      |      |  |

(4) *Mental disorders*.—The number of mentally deficient individuals among the cases is a little above average, but on the whole we have found neither mental disorders nor organic diseases of the nervous system to be predisposing influences (Table II).

TABLE II.—ST. MARK'S HOSPITAL, 1931–1947 (INCLUSIVE)

| Complete prolapse |   |                      |               |
|-------------------|---|----------------------|---------------|
| 215 (adults)      | { | Depressive psychosis | 3 (1 suicide) |
|                   |   | Mentally deficient   | .. 6          |
|                   |   | Epileptic            | .. 1          |

*Treatment*.—Of the 215 cases of prolapse of the rectum in adults, 173 received surgical treatment. Palliative treatment, such as injections, sphincter exercises, &c., was recommended for 23 poor-risk patients; 19 declined any treatment. The 173



the operative mortality is very low, the recurrence rate very high; that rectosigmoidectomy might relieve up to 40% of their prolapse but leaves half that number incontinent, and some with a stricture; that the Moschowitz operation combined with suture of the levator ani has given a very good result in one case for four years.

I am indebted to the staff of St. Mark's Hospital for their permission to review these cases of prolapse of the rectum, and for their advice and assistance. This work has been done throughout in association with Mr. Henry Thompson, to whom I wish to express my thanks.

**Mr. Henry R. Thompson:** Although the problems of partial prolapse of the rectum are by no means solved, I shall deal only with the major disability of complete prolapse.

At St. Mark's in the past ten years, in spite of fewer beds during the war, an annual average of 15 patients with complete prolapse have been operated on; in 1947 and 1948 there were 27 and 28 cases respectively.

The data and figures presented suggest that we have no reason to be satisfied with results. That in the minds of surgeons there is need for a change or addition to the present treatment is apparent in modifications of rectosigmoidectomy and the revival of Thiersch's operation now employed by Mr. Gabriel, and the development of a sling operation, in which the lateral ligaments of the rectum and the recto-vaginal septum are reconstructed, by Mr. Lloyd-Davies.

The six years prior to 1933, studied because of registration facilities, showed that the operations being done at St. Mark's during these years were those described by Mr. Lockhart-Mummery [1] in 1910 and McCann [2] in 1928 or a combination of the two.

Lockhart-Mummery's operation consisted of a posterior, transverse incision between the anus and coccyx; division of the coccygeal attachment of the external sphincter; opening up of the post-rectal space and stripping the back and sides of the rectum from the sacrum and the levatores ani muscles; finally packing the space so formed with vaseline gauze. The intention was to fix the back and sides of the rectum. As Lockhart-Mummery states in his own description of the operation: "It does not fix the anterior wall and in cases where the prolapse is very large I now fix the anterior wall at the same time by a modification of McCann's operation of stitching together the anterior portions of the levator muscles."

McCann's operation described in 1928 gave as its aim a restoration of the "retentive mechanism" without which the bowel would prolapse with each act of defecation, the integrity of the retentive mechanism depending on the power and co-ordinated action of the levatores ani and sphincter muscles. This restoration was achieved through a perineal approach, in front of the rectum, a dissection of the sphincter ani and levatores ani muscles and the insertion of a series of sutures to tighten these muscles and the fascia over the lower end of the rectum. The operation originally described for the cure of prolapse in women has been modified and practised in males.

This then with the addition of a few cauterizations and phenol injections was the therapeutic picture prior to 1933.

In 1933 Miles [3] described to this Society the operation of rectosigmoidectomy and placed amputation of a rectal prolapse on a sound technical footing. Here it appeared was a method of treatment that all were seeking. It was safe, without operative mortality, without complications and with a small recurrence rate only.

In the St. Mark's hospital report of 1933 it is recorded: "... and 6 other cases (of complete prolapse) were treated for the first time by amputation." The impression of Miles' teaching was so great that since that time the operation has been performed almost to the exclusion of all others save for an occasional Lockhart-Mummery's, Moschowitz's [4] or sigmoidopexy performed quite often for a recurrence following rectosigmoidectomy.

This additional and qualifying sentence appears in this same report of 1933: "although this last operation does not attempt to repair the deficiency in the pelvic floor, if thoroughly performed, no further prolapse can occur."

The noted fact that there was no attempt to repair the pelvic floor was as shrewd a misgiving as the suggested impossibility of a recurrence was optimistic.

Fifteen patients had very good results, and apart from a patulous anus in some, it would be difficult to believe that a rectal operation had ever been performed. With reference to these 15 successful rectosigmoidectomies one might say that, apart from the fact that 50% were males, there was no relation to age at onset, or duration of the prolapse. The average length of bowel excised was 2-4 inches.

(4) *Miscellaneous perineal operations*.—This group includes linear cauterization, sphincter plications, and colporrhaphies. Some of the operations were designed to partially relieve the prolapse, and others the incontinence.

As they were neither standard nor accepted operations for prolapse they are not here considered further.

(5) *Sigmoidopexy*.—Fixation of a long pelvic loop of gut to the abdominal wall has not met with success, even when the pouch of Douglas is obliterated at the same time. All have recurred (Table VI).

TABLE VI.—SIGMOIDOPEXY 9 CASES

|                      |         |                                                    |         |
|----------------------|---------|----------------------------------------------------|---------|
| Sigmoidopexy only .. | 7 cases | Sigmoidopexy with obliteration of pouch of Douglas | 2 cases |
| Traced .. .. .       | 6       | Recurred .. .. .                                   | 2       |
| Recurred .. .. .     | 6       |                                                    |         |

(6) *Moschowitz operation*.—Obliteration of the true pelvis by a suturing method with or without ventral fixation of the uterus has been carried out in 9 patients. Of the 6 traced, 1 died, 4 recurred, and 1 has, so far, been successful.

Apart from the three McCann procedures, 13 patients have had the levator ani muscles sutured together (Table VII). This has been performed either at the same

TABLE VII

| Suture of levator ani muscles combined with: | Cases | Recurrence | No recurrence           |
|----------------------------------------------|-------|------------|-------------------------|
| Posterior proctopexy .. .. .                 | 3     | 3          | 0                       |
| Rectosigmoidectomy .. .. .                   | 4     | 2          | 2 { 6 months<br>4 years |
| Colporrhaphy and/or sphincter plication ..   | 4     | 4          | 0                       |
| Moschowitz operation .. .. .                 | 1     | 0          | 1 (4 years)             |
| Sigmoidopexy .. .. .                         | 1     | 1          | 0                       |
| Total                                        | 13    |            |                         |

time as the operations mentioned above, or as a second stage; when combined with rectosigmoidectomy or a Moschowitz operation it has produced an encouraging result.

To summarize, 85% patients with prolapse of the rectum were females. Males are more often affected before the age of 40, and females after that age; childbirth does not appear to be a predisposing factor, nor are functional or organic nervous disturbances.

If all the operations are considered in retrospect (Table VIII) it will be noted that

TABLE VIII.—PROLAPSE OF RECTUM. RESULTS OF 190 OPERATIONS PERFORMED ON 173 PATIENTS AT ST. MARK'S HOSPITAL

| Perineal                                        | Cases | Abdominal                    | Cases |
|-------------------------------------------------|-------|------------------------------|-------|
| Lockhart-Mummery's posterior proctopexy .. .. . | 30    | Sigmoidopexy .. .. .         | 8     |
| Died .. .. .                                    | 1     | Died .. .. .                 | 0     |
| Recurred .. .. .                                | 29    | Recurred .. .. .             | 8     |
| McCann's operation .. .. .                      | 3     | Moschowitz operation .. .. . | 6     |
| Died .. .. .                                    | 0     | Died .. .. .                 | 1     |
| Recurred .. .. .                                | 3     | Recurred .. .. .             | 4     |
| Rectosigmoidectomy .. .. .                      | 108   | No recurrence .. .. .        | 1     |
| Died .. .. .                                    | 0     |                              |       |
| Recurred .. .. .                                | 65    |                              |       |
| No recurrence .. .. .                           | 43    |                              |       |
| Miscellaneous operations .. .. .                | 35    |                              |       |

(Incontinent 21, stricture 4)

the operative mortality is very low, the recurrence rate very high; that rectosigmoidectomy might relieve up to 40% of their prolapse but leaves half that number incontinent, and some with a stricture; that the Moschowitz operation combined with suture of the levator ani has given a very good result in one case for four years.

I am indebted to the staff of St. Mark's Hospital for their permission to review these cases of prolapse of the rectum, and for their advice and assistance. This work has been done throughout in association with Mr. Henry Thompson, to whom I wish to express my thanks.

**Mr. Henry R. Thompson:** Although the problems of partial prolapse of the rectum are by no means solved, I shall deal only with the major disability of complete prolapse.

At St. Mark's in the past ten years, in spite of fewer beds during the war, an annual average of 15 patients with complete prolapse have been operated on; in 1947 and 1948 there were 27 and 28 cases respectively.

The data and figures presented suggest that we have no reason to be satisfied with results. That in the minds of surgeons there is need for a change or addition to the present treatment is apparent in modifications of rectosigmoidectomy and the revival of Thiersch's operation now employed by Mr. Gabriel, and the development of a sling operation, in which the lateral ligaments of the rectum and the recto-vaginal septum are reconstructed, by Mr. Lloyd-Davies.

The six years prior to 1933, studied because of registration facilities, showed that the operations being done at St. Mark's during these years were those described by Mr. Lockhart-Mummery [1] in 1910 and McCann [2] in 1928 or a combination of the two.

Lockhart-Mummery's operation consisted of a posterior, transverse incision between the anus and coccyx; division of the coccygeal attachment of the external sphincter; opening up of the post-rectal space and stripping the back and sides of the rectum from the sacrum and the levatores ani muscles; finally packing the space so formed with vaseline gauze. The intention was to fix the back and sides of the rectum. As Lockhart-Mummery states in his own description of the operation: "It does not fix the anterior wall and in cases where the prolapse is very large I now fix the anterior wall at the same time by a modification of McCann's operation of stitching together the anterior portions of the levator muscles."

McCann's operation described in 1928 gave as its aim a restoration of the "retentive mechanism" without which the bowel would prolapse with each act of defecation, the integrity of the retentive mechanism depending on the power and co-ordinated action of the levatores ani and sphincter muscles. This restoration was achieved through a perineal approach, in front of the rectum, a dissection of the sphincter ani and levatores ani muscles and the insertion of a series of sutures to tighten these muscles and the fascia over the lower end of the rectum. The operation originally described for the cure of prolapse in women has been modified and practised in males.

This then with the addition of a few cauterizations and phenol injections was the therapeutic picture prior to 1933.

In 1933 Miles [3] described to this Society the operation of rectosigmoidectomy and placed amputation of a rectal prolapse on a sound technical footing. Here it appeared was a method of treatment that all were seeking. It was safe, without operative mortality, without complications and with a small recurrence rate only.

In the St. Mark's hospital report of 1933 it is recorded: "... and 6 other cases (of complete prolapse) were treated for the first time by amputation." The impression of Miles' teaching was so great that since that time the operation has been performed almost to the exclusion of all others save for an occasional Lockhart-Mummery's, Moschowitz's [4] or sigmoidopexy performed quite often for a recurrence following rectosigmoidectomy.

This additional and qualifying sentence appears in this same report of 1933: "although this last operation does not attempt to repair the deficiency in the pelvic floor, if thoroughly performed, no further prolapse can occur."

The noted fact that there was no attempt to repair the pelvic floor was as shrewd a misgiving as the suggested impossibility of a recurrence was optimistic.

The safeness of the operation is undoubted; it has been done at St. Mark's Hospital over 150 times without an operative mortality. It has its complications, one of which when left untreated has proved fatal and there are certainly recurrences.

The records at St. Mark's now reveal that there is one patient who has had four rectosigmoidectomies, one who has had the operation on three occasions and nine who have had the operation twice. In the cases that Mr. Hughes and I have been able to follow up we have found a recurrence rate of 60%. Assuming that the operation has indeed been thoroughly performed the possibility of recurrence is very real indeed.

To assess success and failure in malignant disease is relatively easy; the patient is either alive or dead. The assessment of the success or failure in the treatment of rectal prolapse is not so simple. It depends on variable factors:

(1) The ease with which patients adjust themselves to disability. Contentment or gross discomfort may describe two patients' reactions to the same degree of disability.

(2) The investigator's own standards of success or failure.

In this investigation by Mr. Hughes and myself 108 cases of rectosigmoidectomy were traced and of these 92 were personally examined and evidence of recurrence was taken to be a protrusion of the complete rectal wall outside the anus on straining. 16 cases were not seen but were communicated with by letter and the answer "yes" to the question "Does the rectum still prolapse?" was taken as evidence of recurrence.

Ever since 1912 when Moschowitz emphasized the fact that complete prolapse was a sliding hernia of the anterior rectal wall attempts have been made to treat it as such.

The surgical principles of treatment of an inguinal hernia are to remove the sac, repair the fascial defect round the internal ring and narrow the stretched external ring. Applied to a rectal prolapse this implies: removal or obliteration of the pouch of Douglas, repair of the pelvic diaphragm and a narrowing of the stretched anal sphincter.

A rectosigmoidectomy accomplishes none of these essential steps. I have watched, through a laparotomy incision with the patient in the lithotomy Trendelenburg position, the peritoneal suture being inserted by a surgeon performing a rectosigmoidectomy and am convinced that any alteration in the size of the peritoneal pouch is quite negligible in comparison to its total size. It is analogous to removing the fundal tip of a scrotal hernial sac.

There is no repair to the pelvic floor in the standard operation.

A rectosigmoidectomy does not in any way narrow the external sphincter or external ring apart from removing the dilated rectum which is the stretching agent to the sphincter. Contrary to expectation the sphincter frequently does not recover tone.

How then does a rectosigmoidectomy produce results so brilliantly successful in some cases?

(1) The major part of the prolapsing viscus is removed. This as will be seen later may also be a grave disadvantage in other respects.

(2) The sigmoid colon is drawn down and pulled taut, thus a suspension or form of pexy is achieved.

(3) The mesosigmoid is shortened.

(4) Perhaps a fibrosis round the anastomosis site may also give support.

Can the principles of hernia surgery be applied to the problem of rectal prolapse? Firstly, can the hernial sac be removed or obliterated? This desirable step can only be achieved by abdominal operations, i.e. from above. Moschowitz's method of inserting a series of circular thread sutures to obliterate the sac is well known. Roscoe Graham [5] excised redundant peritoneum and resutured the peritoneal floor at a higher level. Mayo erected a scaffolding of fascial strips across the true pelvic brim, the peritoneum being drawn up and sutured over the fascial strips to reconstitute the peritoneal floor at the level of the brim of the pelvis instead of at the pelvic diaphragm.

No appreciable difference can be made to the hernial sac from below. In a recent article by Dunphy [6] a drawing is shown depicting the dissecting up of a sac of peritoneum from below. The posterior wall of the sac is, of course, formed by visceral peritoneum covering the anterior rectal wall. It is impossible to dissect up visceral peritoneum from intestine without removing part of the muscle wall of the bowel as well, and this is impracticable.

Next, can the pelvic floor consisting of the levatores ani and its fascia be repaired? The necessity of doing this has long been appreciated. It may be attempted in three different ways :

(1) As a form of perineorrhaphy from below through the recto-vaginal or recto-perineal approach. Examples of this are McCann's operation, the perineal part of Victor Bonney's operation and recently operations described by Channing Barrett [7].

(2) From above, after incising the pelvic peritoneum as in the operation described by Roscoe Graham. My own experience is that the identification and suturing of levatores ani from above is a difficult and exacting operation both for surgeon and patient, and it is unwise to use this method in the frail and elderly or obese middle-aged patients in whom rectal prolapse may so often be found.

(3) A third way recently practised by Cohn [8], Gabriel [9] and Dunphy is to suture the levatores ani together, as an additional step to a rectosigmoidectomy, through the dilated lower rectal cuff.

Lastly, in the past various plastic operations on the sphincters have been done both in front and behind the rectum with the object of narrowing the hernial external ring. I think it is common experience that the stretched dilated muscle does not take kindly to reconstruction and suturing, and little help can be expected from these measures.

What happens to the sphincter mechanism in cases of complete prolapse? Are there irreversible changes in the sphincter ani muscles in cases of long standing? If a longitudinal section is made through a rectum amputated for prolapse, it may be noted that the circular muscle coat in the region of the prolapse apex is greatly thickened. This thickening is due to œdema of the muscle. In long-standing cases it is possible that this œdema leads to destruction of muscle fibres, fibrosis and loss of contractibility. These changes, most marked at the prolapse apex, may in a lesser degree affect the specialized portion of the circular muscle, the internal sphincter.

In this series, only 20% of cases of rectal prolapse treated by rectosigmoidectomy had normally functioning sphincter mechanism. Most were unable to control fluid fæces or flatus. Many complained of having 5-6 bowel actions first thing in the morning and passing small, hard pellets which rather dropped out than passed in the normal controlled way. In others there was no control at all.

A characteristic finding in cases following rectosigmoidectomy is that there is no resting tone to the sphincter but a fair degree of voluntary contraction. During the course of a rectosigmoidectomy can the sphincter mechanism of the bowel be injured?

In his original description Miles (1933) described an initial longitudinal incision in the prolapse commencing, anteriorly,  $\frac{1}{2}$  inch from Hilton's white line. The object of commencing here was to prevent damage to the external sphincter muscle, especially to the point of fusion between the levator ani and the external muscular coat of the rectum upon which depends subsequent control over the contents of the bowel.

I have not found it easy to identify Hilton's white line on the distended ano-rectum of a complete prolapse. Gabriel gives a point  $\frac{3}{4}$  inch distal to the anal margin as the site of the initial circular incision. To avoid damage to the sphincter mechanism I now favour making the incision through the outer layer of bowel 1 inch below the ano-rectal line, as I consider that subsequent suturing of the bowel margins will probably destroy another  $\frac{1}{2}$  inch of margin as functioning bowel muscle. It also leaves a small additional part of a viscus that from recent work [10] appears essential for the normal working of the sphincter mechanism.

This introduces the last possibility to explain a functionless sphincter. Is it possible that the nerve supply to the sphincter mechanism is destroyed during the operation?

This might be a destruction of the motor efferents or an interruption of the sensory afferents. There is an increasing volume of evidence that the rectum proper is an important receptor organ and that initiating mechanism of the motor activity of the sphincter lies in the rectum, especially in the part immediately above the anal canal. Remove that receptor organ and it is not surprising that the normal reflex mechanism is destroyed and function lost.

An improvement in results may yet be achieved (a) by choosing the most suitable operation or combination of operations for the various types of patients that present for treatment, with the emphasis on saving the rectum from ablation where possible, and (b) where removal of the rectum should seem advisable by leaving at least an inch of rectum adjacent to the anal canal in the hope that the reflex mechanism may be spared.

#### REFERENCES

- 1 LOCKHART-MUMMERY, J. P. (1910) *Lancet* (i), 641.
- 2 McCANN, F. J. (1928) *Lancet* (i), 1072.
- 3 MILES, W. ERNEST (1933) *Proc. R. Soc. Med.*, 26, 1445.
- 4 MOSCHOWITZ, A. V. (1912) *Surg. Gynec. Obstet.*, 15, 7.
- 5 GRAHAM, ROSCOE R. (1942) *Ann. Surg.*, 115, 1007.
- 6 DUNPHY, J. E. (1948) *Surg. Gynec. Obstet.*, 86, 493.
- 7 BARRETT, CHANNING W. (1943) *Amer. J. Surg.*, 59, 519.
- 8 COHN, I. (1942) *Amer. J. Surg.*, 57, 444.
- 9 GABRIEL, W. B. (1948) *Principles and Practice of Rectal Surgery*. 4th Ed., London, page 106.
- 10 GASTON, EUGENE (1948) *Surg. Gynec. Obstet.*, 87, 280, 669.

**Professor C. Formston, F.R.C.V.S.:** Prolapse of the rectum as it occurs in domestic animals is most commonly encountered in the young. It is associated with systemic disease, debility, parasitism and dietetic disorders with diarrhoea as a concomitant feature. Chronic constipation, rectal neoplasms, enlarged prostate and vesical calculus cannot be included as aetiological factors. Haemorrhoids do not occur in animals.

The incidence of prolapse is highest in the puppy, foal and the young pig. In the adult horse several feet of colon may be prolapsed. As in man, the procidentia has to be differentiated from intussusception.

**Diagnosis** presents no difficulty, but in animals not under constant observation the prolapsed bowel is often found to be grossly tumefied, excoriated and frequently shows areas of superficial necrosis. In pigs cannibalistic amputation occasionally occurs before more expert surgical attention can be given. In the same species strangulation and sloughing of the prolapse has been followed by complete recovery.

**Treatment.**—Assuming that attention is given to the causal factors, treatment will vary according to the species, and the degree and condition of the prolapse. In severe cases the only rational treatment is amputation. This method in the pig and dog is singularly successful. In the absence of gross morbid change a simple colopexy is the operation of choice in both the dog and the young pig, although in the latter animal the owner often prefers the more drastic surgical measure of slaughter.

Manual reduction may be difficult or impossible in the foal, and the surgeon may have to resort to the resection of a collar of rectal mucous membrane and the union of the cut edges by suture. This plastic measure facilitates reduction; recurrence is unusual and stricture unknown.

Rectal prolapse is by no means as serious in animals as in man. No doubt this is one compensation for not having adopted the upright position of primates.

**Mr. C. B. O'Carroll:** I have been measuring the pressure at which a normal desire to defæcate is felt, after distending a rubber bag which is inserted into the rectum.

In a small series who have had a rectosigmoidectomy for complete rectal prolapse, I have found that there is no desire to defæcate after a considerable rise in pressure above the normal, or pre-operative level. The patient has, however, observed abdominal pain or discomfort. On slightly deflating the balloon, and extracting it through the anus, it has been found that they do not notice its passage until actually presenting at the anus. It would appear from this preliminary report that in the present operation of rectosigmoidectomy there is interference with the afferent fibres of rectal sensation.

**Mr. O. V. Lloyd-Davies:** The operation of rectosigmoidectomy is tantamount to removing a hernial sac without repairing the deficiency in the muscle and fascial wall and this no doubt accounts for the high recurrence rate shown by the follow-up figures at St. Mark's Hospital.

Another defect of this operation is that, as a rule, patients are far more troubled by bowel function after rectosigmoidectomy than they were before the operation because they receive few, if any, sensations from the pelvic colon which replaces the removed rectum.

In normal cases the desire to defæcate arises from a sensation of fulness in the rectum produced by an increase of pressure within the lumen and also from a feeling of pressure or weight upon the pelvic floor.

In prolapse cases the sphincter tone is so poor that it is very doubtful whether they are able to receive any sensations from increase in intraluminal pressure and in all probability they rely upon sensations derived from the pelvic floor.

These rectal sensations are most important to the patient, a fact which strongly supports the view that the rectum should not be excised and that the problem should be tackled by repairing the deficiency in the pelvic floor and by giving the rectum adequate support.

When performing a laparotomy upon female cases with a complete rectal prolapse the following features are constantly found.

*First:* The very deep pelvic peritoneal pouch of Douglas which extends through the anal orifice when the prolapse is down.

*Secondly:* There is no recto-vaginal septum and the perineal body is very attenuated.

*Thirdly:* The mesentery of the rectum is far less bulky than normal since it contains less fat. It is largely peritonealized throughout its course like the pelvic mesocolon, and the rectum can be lifted freely from the anterior surface of the sacrum.

*Fourthly:* There are no lateral ligaments. The peritoneum on either side of the lowest part of the bowel where it passes forwards to the pelvic aperture rests upon the superior surface of the levators with only a thin intervening layer of fat.

#### THE OPERATION

To produce an operation which will effectively prevent any recurrence of the prolapse it would appear to be necessary to obliterate the deep pelvic peritoneal pouch, reform the recto-vaginal septum and also produce new lateral ligaments which will firmly tether the rectum.

An abdominal approach is necessary to accomplish this efficiently.

In a small series of cases I have placed six floss silk slings between the rectum and the vagina. The slings are firmly attached at the sides of the rectum by taking a good bite of the sacrospinous ligaments.

These slings are relatively loosely tied in front in order not to constrict the anterior rectal wall.

Each sling is now placed at approximately half-inch intervals between the rectum and vagina and held in position by stitching the anterior rectal wall to the posterior vaginal wall with non-absorbable sutures.

The lowest sling is placed at the level of the perineal body and the uppermost at the level of the supravaginal portion of the cervix.

When the slings have been placed in position a fanlike framework of silk will be seen passing on either side of the rectum to the sacrospinous ligaments.

This produces a strong and stout recto-vaginal septum and considerable fibrosis laterally, thus forming new lateral ligaments.

The operation is completed by obliterating the pelvic peritoneum at the sides of the rectum by non-absorbable purse-string sutures after the method of Moschowitz. When it appears necessary the round ligaments may be shortened and fixed.

The first operations in this series were for cases which had recurred after rectosigmoidectomy but the last four cases have not had a previous rectosigmoidectomy. So far the results in all the cases have been very satisfactory.

Unfortunately the operation is a major one and therefore unsuitable for elderly patients.

For the elderly some modified operation will have to be devised to obliterate from the perineum as much as possible of the peritoneal pouch and at the same time reduce the size of the pelvic aperture by bringing the levators together with non-absorbable suture material.



## Section of Ophthalmology

President—CHARLES GOULDEN, O.B.E., M.A., M.D., F.R.C.S.

[June 9, 1949]

### Optic Nerve Compression and its Differential Diagnosis

By S. P. MEADOWS, M.D., F.R.C.P.

OPTIC nerve compression is of interest to the ophthalmologist, neurologist, and neurosurgeon. Like many such problems it lies on the borderland between ophthalmology and neurology. Nor is the subject one of clinical interest only, for we are by no means certain of the cause of the pallor of the optic disc which ensues after prolonged intracranial compression of the optic nerve. It is said to be due to disappearance of the capillaries in the optic disc, and may be of vascular origin consequent on compression of the nerve. The term optic atrophy infers degeneration of the optic nerve, and yet we use it as a clinical term to indicate the appearance of the optic disc, when we should perhaps speak of optic disc pallor.

I wish to refer to the clinical aspects of optic nerve compression, and to a group of cases in which unilateral compression occurs as the initial manifestation. The literature on this subject is scanty. Cushing (1938), in describing meningiomas of the inner portion of the sphenoidal ridge, refers to the unilateral failure of vision in association with a "primary" optic atrophy, which may occur, and progress to near blindness, before the other eye becomes involved. McKendree and Doshay (1936) describe 6 cases of optic nerve compression, 3 meningiomas and 3 aneurysms, in several of which the compression was predominantly unilateral. Schlezinger, Alpers and Weiss (1946) describe 4 cases of suprasellar meningioma in which the initial compression was of the optic nerves, instead of the more usual chiasmal involvement. The authors refer to the expanding scotomatous or sector defect in the visual fields which is so typical of optic nerve compression, though in none of their cases was the compression predominantly unilateral. Foster Moore (1925) describes a mycotic aneurysm of the ophthalmic artery which presented with monocular blindness of sudden onset. Jefferson (1937) refers to compression of the optic nerves by aneurysms, but from his recorded cases it appears that aneurysms rarely present with unilateral optic nerve compression alone. Other structures, such as the optic chiasm or tract, or the oculomotor nerves, are usually involved as well.

When pressure is exerted initially on the optic chiasm, as in cases of pituitary adenoma or suprasellar meningioma, the early bitemporal character of the field defect usually gives a clue to the localization of the lesion, although there may be later evidence of optic nerve compression as well. When the initial compression involves the optic nerves, however, as in anteriorly situated basal meningiomas, bilateral visual failure and optic atrophy

may be the only presenting clinical features, and diagnosis may be by no means easy, especially when other signs are absent. Anosmia would, of course, assist in the diagnosis of an olfactory groove meningioma, and the presence of unilateral exophthalmos would indicate a space-occupying lesion, and occurs, for instance, in cases of optic nerve tumours and meningiomas involving the sphenoidal ridge. The presence of unilateral visual failure with a pale disc, in association with papillædema in the other eye, is also a well-established clinical syndrome in frontal tumours (Foster Kennedy syndrome). I mention these well-known accompaniments of optic nerve compression, as they were little in evidence in the present series of cases.

The group of cases I propose to discuss consists of those in which optic nerve compression occurs as the early and presenting feature, and in which the compression is predominantly or entirely unilateral. From the clinical aspect it will be realized that these cases offer considerable difficulty in diagnosis, and it is this aspect to which I wish to refer in particular.

The 11 cases on which this communication is based consist of 7 basal meningiomas, 3 aneurysms or vascular anomalies, and 1 glioma of the optic nerves and chiasm. It is, of course, not unknown for a pituitary adenoma to present with unilateral optic nerve compression, instead of the usual chiasmal features; for a nasopharyngeal neoplasm on rare occasions to appear with a similar clinical picture, instead of the more usual oculomotor and trigeminal involvement; and for an arteriosclerotic and tortuous internal carotid or ophthalmic artery to mimic a tumour or aneurysm by compressing the optic nerve. How often this last occurs is conjectural, for if such a condition is suspected, intracranial exploration is usually avoided, especially in the older age-group. I have seen a tortuous carotid artery result in compression of the optic tract, and mimic a tumour to a nicety, and it may well be that optic nerve compression by a pathological artery, without aneurysmal formation, is more frequent than we realize. Sunderland (1948) refers to this subject when discussing neurovascular relations at the base of the brain, and shows a photograph of a tortuous and atheromatous carotid artery compressing one optic nerve. I have avoided mentioning cases of intracranial tumour in which optic nerve compression occurs as a late phenomenon, as such cases present less difficulty from a diagnostic aspect.

It is of interest that all the cases reported here are basal meningiomas, or aneurysms, with one glioma of the chiasm and optic nerves. This is perhaps to be expected, since basal meningiomas and aneurysms are often so placed as to be likely to come in contact with the optic nerve early in their development. An inferior frontal or temporal glioma can compress or invade the optic nerves, and this subject has been fully discussed by Jefferson (1945) in his Doyne lecture. Involvement of one optic nerve, however, is probably rare as an initial or presenting feature in gliomas. Jefferson (1945) states that the Foster Kennedy syndrome, other things being equal, is itself evidence in favour of a meningioma, as opposed to a glioma, though not exclusively so, but that when one disc is atrophic and the other normal, the probabilities of meningioma are greatly increased.

#### CLINICAL FEATURES

The first effect of optic nerve compression is unilateral visual failure. This is usually of gradual onset, but is occasionally more sudden, particularly in aneurysmal compression. Further, an early peripheral loss of field may pass unnoticed, and the patient may state that the loss of vision was sudden when the macular fibres become affected later on. I mentioned this apparent abrupt onset which occasionally occurs, as it may lead to a diagnosis of retrobulbar neuritis, as will be described later.

The macular fibres form a large proportion of the optic nerve, and appear to be particularly vulnerable in optic nerve compression. The visual field defect in early cases may consist of a central scotoma, but by the time the patient first consults his medical adviser there is often a gross *central scotomatous defect breaking through to the periphery at one point*; so that all that may remain of the visual field is a peripheral crescentic area of relatively intact vision. This was of particularly common occurrence in the present series of cases (figs. 1, 4, 5, 7, 11). Later, of course, the eye becomes blind, and the patient then presents himself with monocular blindness and optic atrophy.

Traquair (1946) states that central vision is nearly always reduced in cases of optic nerve compression, and that a central scotoma is common. He also refers to the frequency of a wide sector depression of the field, of irregular quadrantic or hemianopic shape.

In a recent paper (published after the present communication was given) Mooney and McConnell (1949) state that a central scotoma is particularly liable to occur when the optic nerve is elevated or depressed in the region of the optic foramen, and refer to the possible mechanisms, such as pressure of the nerve against the margin of the optic foramen, or pressure on, or kinking of, the ophthalmic artery. Case IV in their paper is similar to the cases in the present series, in presenting with unilateral central scotoma and optic atrophy, due to a probable aneurysm lifting up the optic nerve. They also refer to the rarity of a central scotoma in cases of pituitary adenoma, though the latter frequently lies between the optic nerves and presumably exerts pressure on these structures, as well as on the chiasm.

*Visual hallucinations* in the affected eye were present in one patient at the onset (Case X), in association with fairly rapid unilateral visual failure. This patient, an elderly woman, noticed "sudden lights in front of the right eye, like blue stars with a red rim". Some hours later a grey mist appeared in the temporal field of the right eye, and within a short time the eye was almost blind, but a small area of vision remained in the peripheral field above. The visual hallucinations lasted a day or so. Some months previously she had noticed a sudden beating noise in her head, which persisted, being more marked on exertion. The aneurysmal or vascular nature of the optic nerve compression seemed almost certain, as a loud systolic bruit was heard on auscultation of the right eye and head, which was abolished by pressure on the right common carotid artery in the neck.

The *optic fundus* may show no abnormality if the patient is seen early. Later, it is usual to find a progressive pallor of the disc, though it may be several months before this is evident. Papilloedema was observed in one patient as a temporary phenomenon early in the course of the compression (Case X). At this stage the patient was almost blind in the eye, though with a localized sparing of a part of the peripheral field, thus mimicking a case of retrobulbar neuritis very closely, were it not that an ocular bruit was heard with a stethoscope. What appears to be a very rare mode of presentation—and I have not seen it described in the literature—is that of a central retinal venous thrombosis. This was the first clinical evidence of optic nerve compression in one patient (Case XI), and was followed by thrombotic glaucoma and enucleation of the eye. The patient was referred to me with a temporal hemianopia in the remaining eye, and proved to have a glioma involving both optic nerves and chiasm.

In addition to involvement of the vision of the ipsilateral eye, pressure on the posterior or chiasmal extremity of the optic nerve may involve the *crossed nasal fibres from the other eye*, which pass forwards into the posterior extremity of the optic nerve before passing back into the tract. From clinical observations

it seems likely that the lower crossed nasal fibres are particularly prone to be affected by pressure at this situation (Diagram A), with consequent defect in the periphery of the opposite upper temporal field. In one of the present series of cases, the appearance of this upper temporal defect in the other eye was the first almost certain proof that a unilateral optic atrophy was due to pressure, and exploration revealed a large meningioma arising from the tuberculum sellæ (Case III, fig. 6).

Further, a *partial crossed homonymous defect* in the contralateral fields, which may be confined to the upper or lower quadrants, can occur in association with a severe central loss of vision in the ipsilateral eye, and is probably suggestive of aneurysm. This feature was present in two of this series of cases (figs. 13, 15), both probably aneurysms, and has been mentioned by Jefferson (1937). This clinical picture infers that the aneurysm is large enough to affect both optic nerve and optic tract on one side.

I have described the effect of optic nerve compression on the vision, fields, and optic fundus, and I would now like to refer to the question of pain. In several cases of proved meningioma with unilateral optic nerve compression, the *absence of pain and headache* has been a striking feature (Cases I and III). In Case I, a male aged 27, unilateral visual loss of fairly sudden onset had appeared ten years

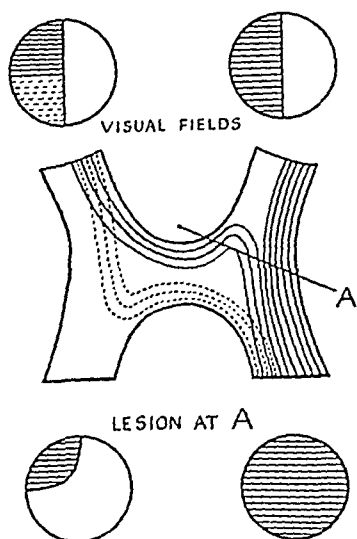


DIAGRAM A.—To show probable course of crossed nasal fibres in optic chiasm, and field defect due to a lesion at A, as in Case III. (Continuous line represents lower nasal fibres, and interrupted line represents upper nasal fibres.)

previously at the age of 17, and a central scotomatous defect had persisted over this period, without any pain. The original diagnosis had been that of acute retrobulbar neuritis. After ten years, headaches and vomiting appeared fairly suddenly, and exploration revealed a large meningioma in the suprasellar region. In Case III, a male aged 49, there had been progressive failure of the vision of the right eye over a period of no less than five years, with no history of headache or pain. The difficulty in diagnosis in this case is, perhaps, emphasized by the fact that the following diagnoses had been suggested at different times during the five years: chronic glaucoma, chiasmal arachnoiditis, an unusual retrobulbar neuritis, hæmorrhage into the optic nerve, and pituitary tumour. X-rays of the skull and optic foramina were normal. The appearance of a slight defect in the upper temporal field of the normal eye five years after the onset of symptoms gave a clue to the diagnosis, and exploration revealed a large suprasellar menin-

gioma arising from the tuberculum sellæ. The absence of pain needs emphasis, perhaps, as it may direct one's thoughts away from a tumour as the cause of monocular blindness. On the other hand, cases of optic nerve compression due to aneurysm often have a history of severe pain, sometimes early in the history and temporary only, and the significance of this early episode may be missed when the patient appears later with a painless blind eye and optic atrophy (Case VIII). Yet even in aneurysmal compression of the optic nerve pain may be entirely absent.

A systolic cephalic bruit, best heard by auscultation over the eye, is occasionally heard in aneurysmal cases; it may be diminished or abolished by compression of the ipsilateral carotid artery in the neck (Case X). The absence of a bruit does not exclude aneurysm. It is more commonly absent than present.

The clinical course of many of these cases is of interest. It will be seen from the case histories that the length of history during which the only sign is unilateral loss of vision may extend to a period of several years, particularly in cases of meningioma (ten years in Case I, and five years in Case III). This fact, perhaps, needs emphasis, especially as the early stages may be entirely painless. In some cases, too, the clinical state may appear to be static over a prolonged period, and can be misleading (Case I). The appearance of a slight defect in the peripheral temporal field of the sound eye is of great diagnostic importance, and is an almost certain proof of compression as the cause of the unilateral visual failure (Case III).

In aneurysmal compression there may be an improvement in the vision, quite apart from the effect of surgical treatment. In one patient (Case VIII) who had an aneurysm pressing on one optic nerve, there was a central scotoma, and vision was reduced to "counts fingers" in this eye. About a year later, without any radical treatment, though there had been an intracranial exploration, the vision had improved to 6/9 and the central scotoma had disappeared.

#### ACCESSORY METHODS OF INVESTIGATION

These include radiographic examination of the skull and optic foramina, examination of the cerebrospinal fluid, arteriography and ventriculography. Radiography of the skull may show evidence of hyperostosis, as in meningiomas arising from the sphenoidal ridge, tuberculum sellæ or olfactory groove, or there may be evidence of localized bone erosion, and even calcification within the meningioma. An aneurysm may show evidence of calcification in its wall. Enlargement of the optic foramen occurs when an optic nerve tumour, glioma or meningioma, has an intra-orbital and an intracranial portion. Arteriography by the percutaneous method is indicated when an aneurysm is suspected, and is a relatively safe procedure. It is, however, of considerable use in tumour cases, as the arteries may be displaced by a tumour, or the meningioma itself may take up the radiopaque substance, outlining itself clearly by the so-called "blush" (Case VI, fig. 10). Ventriculography is usually indicated in tumour cases, when displacement or deformation of the anterior horns or of the third ventricle may be seen in cases of large basal meningiomas.

One would expect that further investigation on these lines would clear up any doubts as to the diagnosis. But this is by no means always the case, especially when investigations are undertaken early in the course of the condition. Ventriculography may be normal when a tumour is small enough not to deform the ventricles, and, of course, it is in precisely such a case that one would expect operative results to be best (Case V). Arteriography may also be quite negative in the case of an undoubted aneurysm, either because of clotting in the wall of the aneurysm, or when the aneurysm is not in direct continuity with one of the main

vessels (Case VIII). The corollary seems to be that if optic nerve compression is suspected and all investigations are negative, then intracranial exploration of the optic nerve is justifiable. This happened in 3 of the present series of cases. In one case a small meningioma was found arising from the anterior clinoid process, and was completely removed, with recovery of vision from hand movements to 6/9 within three weeks (Case V). In another (Case IV), there was a plaque of meningioma surrounding one optic nerve. A small aneurysm was found in a third case, which did not show on arteriography (Case IX).

#### DIFFERENTIAL DIAGNOSES

The most likely condition which is apt to be confused with unilateral optic nerve compression is unilateral retrobulbar neuritis. In this condition the onset is usually abrupt, a central or paracentral scotoma is present, and the fundus may be normal or the disc slightly swollen. Pain is frequently present, and tenderness of the globe common. Recovery of vision during the following few weeks is the rule. I should recall, however, that pain is sometimes absent, and that occasionally there may be little or no recovery in the vision, so that the patient is left with a permanent defect in the central field, usually associated with a pale disc. It is this type of case in which diagnosis from optic nerve compression may be one of extreme difficulty. One must remember, too, that optic nerve compression by an aneurysm may be painful and abrupt, and even associated with swelling of the optic disc in the early stage (Case X), and the defect in vision may even improve (Case VIII), thus closely mimicking retrobulbar neuritis. The point of practical importance is to remember the possibility of optic nerve compression in the case of a supposed retrobulbar neuritis of unusual type, where the vision does not clear. This difficulty does not often arise, but, as will be realized, early operation in optic nerve compression may lead to complete recovery of vision (Case V), whereas if we leave a doubtful case and observe masterly inactivity, it may prove almost impossible, at a later date, to remove a large meningioma (Case I). In 2 of the present series, both cases of meningioma, the early presence of a central scotoma of fairly abrupt onset, with optic atrophy, led to a provisional diagnosis of retrobulbar neuritis. In one of these patients (Case II), further observation showed that the scotoma was gradually extending to the periphery, and exploration was undertaken. In the other patient (Case I), a youth of 17, the vision and scotomatous defect appeared to have changed little, if at all, over a period of ten years, when headaches and vomiting appeared, by which time the tumour was very large indeed.

The only other conditions likely to be confused with optic nerve compression are vascular lesions of the retina and optic nerve, and chronic glaucoma. The vascular groups include narrowing of the retinal arterial tree, with sudden occlusion or more gradual ischæmia, in addition to vascular lesions of the nerve, about which our knowledge is scanty. As mentioned previously, a tortuous and sclerotic carotid artery may also involve the optic nerve. It would be unwise for a physician to refer to glaucoma, except to state that such a condition has been known to appear in the neurological or neurosurgical wards as a suspected intracranial tumour. In one recent case, not included in this series, which I suspected of having a meningioma or aneurysm compressing the optic nerve, surgical exploration revealed evidence of arachnoiditis of the chiasm and optic nerve. We know little about this condition, and unless it has been proved by inspection, such a diagnosis should be viewed with suspicion.

In conclusion I would emphasize that unilateral visual failure with a central scotomatous or sector defect may be the presenting feature of a basal meningioma or aneurysm, that the onset may be gradual or fairly sudden, and that there may

be a complete absence of headache and pain. The history may go back many years without any abnormality other than unilateral blindness and optic atrophy, and negative investigations should not deter us from considering intracranial exploration.

### CASE RECORDS

*CASE 1.—Unilateral visual failure and optic atrophy of ten years' duration caused by meningioma arising from diaphragma sellae.*

W. C., male, aged 27. Early in 1938 he noticed a fairly rapid loss of vision of the left eye, especially in the centre of the field. He had no headaches or pain. Examination seven months after the onset revealed left optic atrophy, with vision reduced to 6/60. There was a central scotoma with full peripheral fields. The left pupil reacted fairly briskly to light. The nervous system appeared otherwise normal.

The condition appeared to remain almost stationary till 1948, i.e. for ten years, during which period his general health was excellent. Even in 1944, six years after the onset, visual acuity in the left eye was still 3/60, with a left central scotoma. In August 1948 the patient developed generalized headache and vomiting, occurring several times weekly. Examination in October 1948 showed primary optic atrophy in the left eye and slight pallor of the right optic disc. In the left eye vision was reduced to hand movements in the temporal field only, the right visual acuity being 6/6. The left visual field was reduced to a crescentic area in the periphery of the temporal field, while there was a slight defect in the periphery of the right upper temporal field (fig. 1). The left pupil reacted poorly to direct light, but well consensually. The nervous system was otherwise normal.

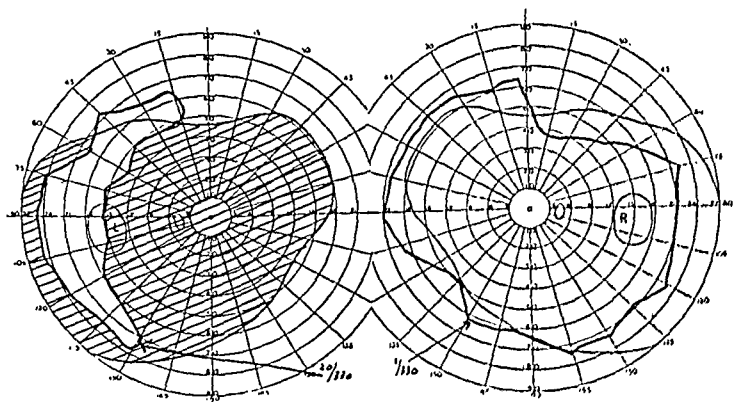


FIG. 1.—Visual fields of Case I, ten years after onset of unilateral visual failure, showing early defect in upper temporal field of contralateral eye.

Examination of the cerebrospinal fluid in 1948 showed a slightly raised pressure (170 mm.), a total protein of 110 mg.%, and a positive globulin test, but the cell count was normal and the Wassermann reaction negative. Radiography of the skull revealed destruction of the dorsum sellae and posterior clinoid processes, with normal anterior clinoid processes and optic foramina. Ventriculography revealed gross symmetrical hydrocephalus of the lateral ventricles, with lack of filling of the third ventricle.

On November 19, 1948, operation by Mr. Valentine Logue revealed a large hard tumour extending forwards and laterally from the region of the sella turcica, and so distorting the left optic nerve and chiasm that they could not be identified. The site of the origin of the tumour could not be identified for certain, but was probably the diaphragma sellae (figs. 2 and 3). No radical treatment was possible. On microscopy the tumour proved to be a slowly growing meningioma.

vessels (Case VIII). The corollary seems to be that if optic nerve compression is suspected and all investigations are negative, then intracranial exploration of the optic nerve is justifiable. This happened in 3 of the present series of cases. In one case a small meningioma was found arising from the anterior clinoid process, and was completely removed, with recovery of vision from hand movements to 6/9 within three weeks (Case V). In another (Case IV), there was a plaque meningioma surrounding one optic nerve. A small aneurysm was found in a third case, which did not show on arteriography (Case IX).

#### DIFFERENTIAL DIAGNOSES

The most likely condition which is apt to be confused with unilateral optic nerve compression is unilateral retrobulbar neuritis. In this condition the onset is usually abrupt, a central or paracentral scotoma is present, and the fundus may be normal or the disc slightly swollen. Pain is frequently present, and tenderness of the globe common. Recovery of vision during the following few weeks is the rule. I should recall, however, that pain is sometimes absent, and that occasionally there may be little or no recovery in the vision, so that the patient is left with a permanent defect in the central field, usually associated with a pale disc. It is this type of case in which diagnosis from optic nerve compression may be one of extreme difficulty. One must remember, too, that optic nerve compression by an aneurysm may be painful and abrupt, and even associated with swelling of the optic disc in the early stage (Case X), and the defect in vision may even improve (Case VIII), thus closely mimicking retrobulbar neuritis. The point of practical importance is to remember the possibility of optic nerve compression in the case of a supposed retrobulbar neuritis of unusual type, where the vision does not clear. This difficulty does not often arise, but, as will be realized, early operation in optic nerve compression may lead to complete recovery of vision (Case V), whereas if we leave a doubtful case and observe masterly inactivity, it may prove almost impossible, at a later date, to remove a large meningioma (Case I). In 2 of the present series, both cases of meningioma, the early presence of a central scotoma of fairly abrupt onset, with optic atrophy, led to a provisional diagnosis of retrobulbar neuritis. In one of these patients (Case II), further observation showed that the scotoma was gradually extending to the periphery, and exploration was undertaken. In the other patient (Case I), a youth of 17, the vision and scotomatous defect appeared to have changed little, if at all, over a period of ten years, when headaches and vomiting appeared, by which time the tumour was very large indeed.

The only other conditions likely to be confused with optic nerve compression are vascular lesions of the retina and optic nerve, and chronic glaucoma. The vascular groups include narrowing of the retinal arterial tree, with sudden occlusion or more gradual ischæmia, in addition to vascular lesions of the nerve, about which our knowledge is scanty. As mentioned previously, a tortuous and sclerotic carotid artery may also involve the optic nerve. It would be unwise for a physician to refer to glaucoma, except to state that such a condition has been known to appear in the neurological or neurosurgical wards as a suspected intracranial tumour. In one recent case, not included in this series, which I suspected of having a meningioma or aneurysm compressing the optic nerve, surgical exploration revealed evidence of arachnoiditis of the chiasm and optic nerve. We know little about this condition, and unless it has been proved by inspection, such a diagnosis should be viewed with suspicion.

In conclusion I would emphasize that unilateral visual failure with a central scotomatous or sector defect may be the presenting feature of a basal meningioma or aneurysm, that the onset may be gradual or fairly sudden, and that there may



spreading to the periphery in the lower nasal field (fig. 4). Visual acuity fell to 6/60 in the right eye. The left visual field was full, though the left optic disc appeared slightly pale.

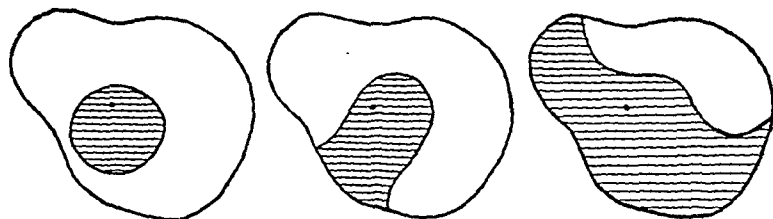


FIG. 4.—Diagram of progress of visual field defect in Case II.

Lumbar puncture was performed in December 1944, when the pressure was raised to over 300 mm. The cerebrospinal fluid was quite normal, the total protein being 15 mg.%. Radiographic examination of the skull at this time showed evidence of erosion of the base of the skull in front of the anterior clinoid processes, with rarefaction of the posterior clinoid processes.

Ventriculography performed on January 22, 1945, showed the presence of a large left frontal tumour, extending across the mid-line. Operation on the same day, by Mr. Wylie McKissock (left frontal approach), revealed an enormous left frontal meningioma, which appeared to arise from the anterior end of the falx cerebri, and one large lobule of tumour extended beneath the falx. The latter was the obvious cause of the loss of vision in the right eye. The tumour was completely removed. Convalescence was uninterrupted.

The patient was last seen in February 1949, four years after operation, when she was fit and well. There was right-sided optic atrophy, with visual acuity less than "counts fingers". The right visual field showed little change from its pre-operative state (fig. 5). The left visual acuity was 6/6.

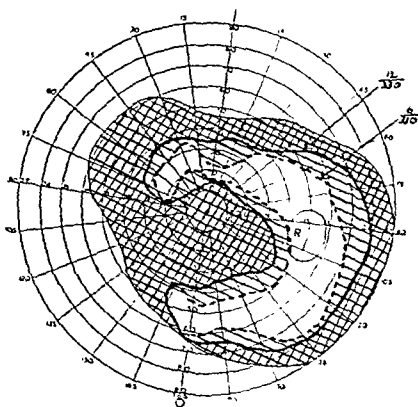


FIG. 5.—Visual field of Case II, three and a half years after removal of meningioma compressing the right optic nerve.

### CASE III.—Meningioma of tuberculum sellæ, with monocular blindness.

P. R., male, aged 49, complained of progressive failure in the vision of the right eye over a period of about five years, since 1943. In December 1943, it was reported that there was a defect in the upper temporal field, and that visual acuity was reduced to 6/60. At one time he was reported to show a defect in the upper nasal quadrant suggestive of chronic glaucoma. There had been no headaches or pain, and his general health had remained good.

The following diagnoses had been suggested during this progressive visual failure: chronic glaucoma, chiasmal arachnoiditis, an unusual retrobulbar neuritis, hæmorrhage into the optic nerve, and pituitary tumour.

Examination in December 1946 showed well-marked primary optic atrophy on the right side, with visual acuity reduced to counting figures in the lower nasal field. There was no vision in the temporal or upper nasal field or at fixation point. The right pupil reacted poorly to direct light, but well consensually. Sense of smell was normal, and there were no other abnormal signs in the nervous system.

After a course of radiotherapy, a second surgical exploration was undertaken in April 1949, when the left frontal lobe was amputated. The tumour was seen to consist of three large lobes. One occupied the whole of the sella turcica, and had displaced the pituitary gland and infundibulum posteriorly; a second lobe projected under the left frontal lobe; and a third lobe projected backwards and upwards into the third ventricle. The left optic nerve was a thin band 0.75 cm. across and about 2.5 cm. in length, firmly adherent and incorporated in the tumour capsule, from the optic foramen to the chiasm. The latter had been pushed backwards and was closely applied to the posterior extremity of the tumour. The right optic nerve was stretched round the right side of the tumour. The tumour was removed entirely, after dividing the left optic nerve at the optic foramen and just in front of the chiasm. The patient died forty hours after operation from hypothalamic disturbance.

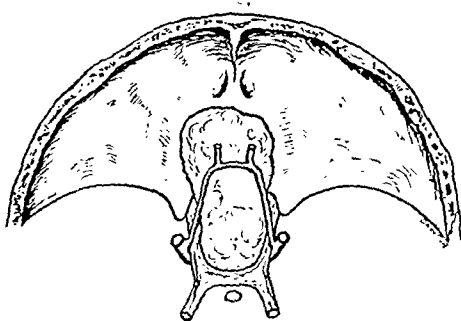


FIG. 2.

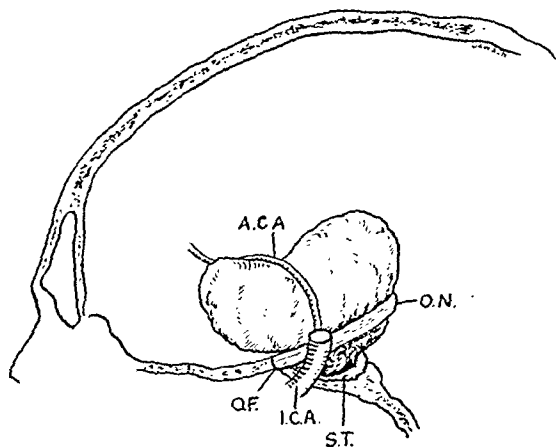


FIG. 3.

A.C.A. Anterior cerebral artery. O.N. Optic nerve.  
O.F. Optic foramen. I.C.A. Internal carotid artery.  
S.T. Sella turcica.

FIGS. 2 and 3.—Diagrams of operative findings in Case I, showing tumour lying between optic nerves, and displacing the optic chiasm backwards.

*Comment.*—This patient was first seen before one had become wise to the clinical picture. The extraordinary feature was the relatively static clinical condition for a period of over ten years, with visual loss confined to one eye. The late surgical intervention showed how large and difficult these meningiomas may become, and stresses the need for early exploration at a stage when the tumour is operable.

*CASE II.*—Meningioma of anterior end of falx cerebri with unilateral optic atrophy and central scotoma.

M. C., female, aged 46. About Christmas 1943 the patient noticed a black spot just below the centre of vision of the right eye, which slowly enlarged in size to involve most of the lower part of the right visual field. There had been no pain associated with the loss of vision, but the patient had had periodic headaches for many years, though she had been free from them for a long period till quite recently, when they recurred. Her general health had remained excellent.

Examination in April 1944, four months after the onset, showed a fairly dense scotoma below fixation in the right visual field, which did not quite reach the periphery of the field below. The right optic disc was moderately pale, and the right visual acuity 6/36 uncorrected. The rest of the examination of the nervous system was normal. Radiographs of the skull and optic foramina were normal.

During the succeeding six months the visual field defect in the right eye spread upwards to involve fixation, and downwards to the periphery of the field, i.e. a large central scotoma

this region, nor of any abnormality of the ventricular system. A right percutaneous carotid arteriogram showed good filling of the internal carotid, anterior and middle cerebral arteries, with no abnormality. The electro-encephalogram was normal.

In view of these negative findings, it was decided to explore the region of the right optic nerve, and this was undertaken by Mr. Wylie McKissock on August 4, 1949. There was a plaque of pinkish-red vascular meningioma arising from the bone immediately above and in front of the sella, and from the anterior wall. A small nodule of tumour extending back to the sella, lying between the optic nerves. The tumour extended two-thirds round the right optic nerve, from within downwards, and the whole removal of the tumour could not be achieved. Microscopy of the tumour proved it to be a meningeal endothelioma.

*CASE V.—Meningioma arising from anterior clinoid process presenting as monocular blindness, with negative investigations, including air studies. Post-operative recovery of vision to 6/9.*

R. T., female, aged 36. In July 1946 the patient noticed gradually increasing loss of vision of the right eye, and within three months the eye was almost blind. The vision in the left eye remained unaltered. Neither pain nor headache had been prominent symptoms. At the onset there had been occasional aching pain behind the right eye and in the right cheek, and she had also had occasional right temporo-occipital headaches since the vision began to fail. There had been no vomiting, and no other symptoms referable to the central nervous system except that her sense of smell had never been good. Her general health had remained good.

Examination in March 1947 showed slight pallor of the right optic disc, and vision in the right eye was reduced to hand movements in the upper field (fig. 7). The right visual field

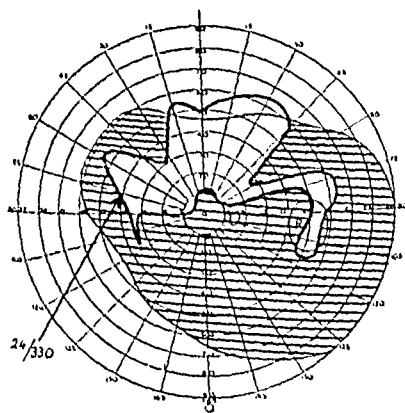


FIG. 7.—Visual field of Case V, before operation.

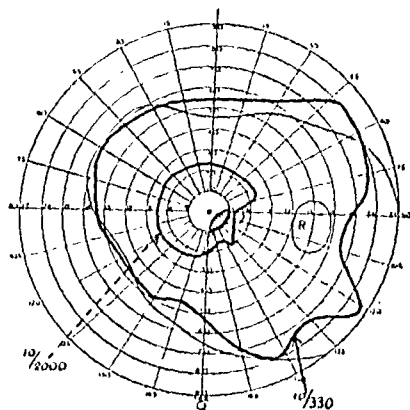


FIG. 8.—Visual field of Case V, three weeks after removal of meningioma.

showed severe loss centrally and inferiorly, the only intact vision being in the periphery of the upper nasal field. The right pupil reacted poorly to direct light but well consensually. On the left side, the optic fundus was normal, the visual field full, and visual acuity 6/5. Ocular movements were full, and there was no exophthalmos. Sense of smell was diminished on the right side, but normal on the left side. There were no further abnormal signs in the central nervous system or elsewhere.

Further investigation showed normal skiagrams of the skull and optic foramina, normal cerebrospinal fluid (pressure 150 mm.), and negative blood Wassermann reaction. Air encephalography showed good filling of a normal cerebral ventricular system.

On May 30, 1947, operation was undertaken, in spite of the negative results of investigations (Mr. Harvey Jackson). A right frontal bone flap was turned downwards, the dura incised and the right frontal lobe elevated. A small meningioma, measuring 2 cm. long by 1 cm. wide, was found arising from the upper surface of the right anterior clinoid process

Skiagrams of the skull and optic foramina in January 1947 showed no abnormality of the optic foramina, clinoid processes, or sella.

In June 1948 he was examined again. The right eye was quite blind. There was now a slight defect in the upper temporal field of the left eye (fig. 6), and the left optic disc had become slightly pale. The left visual acuity was 6/5.

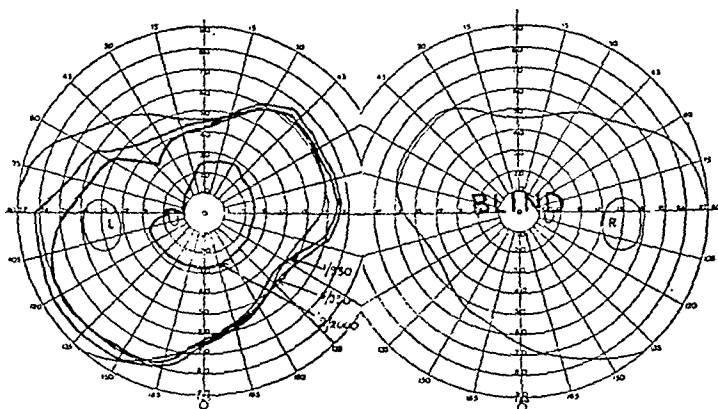


FIG. 6.—Visual fields of Case III, showing monocular blindness and early defect in upper temporal field of contralateral eye.

Investigations in hospital (July 1948) showed that the cerebrospinal fluid was under slightly increased pressure (170 mm.) and the content was normal except for a slight rise in protein (50 mg.%). Skiagrams of the skull showed ? hyperostosis of the tuberculum sellæ.

Ventriculography (July 17, 1948) showed normal lateral ventricles, and a very narrow third ventricle. Myodil ventriculography was therefore performed, and 0.75 c.c. of myodil was injected into the lateral ventricle and manipulated under the screen into the third ventricle. This showed a filling defect in the optic recess, strongly suggestive of a meningioma growing from the tuberculum sellæ.

On July 19, 1948, Mr. McKissock explored the region of the tuberculum sellæ by a right frontal approach. Elevation of the frontal pole revealed a typical suprasellar meningioma lying in the mid-line, and measuring  $2\frac{1}{2}$  inches in each direction. The tumour arose from a circular area of the tuberculum sellæ extending from one optic foramen to the other, and backwards into the sella. Amputation of the frontal pole of the brain was necessary before the tumour could be removed. The tumour was pressing on both optic nerves, the right being splayed out and destroyed by the tumour. Histological examination showed the tumour to be a meningioma.

He developed temporary diabetes insipidus after operation. There was no change in the clinical signs after operation, the left visual acuity remaining good.

**CASE IV.—Meningioma en plaque, presenting with monocular blindness, with negative investigations, including ventriculography and angiography.**

G. V., female, aged 51. In May 1948, thirteen months before examination, the patient noticed progressive deterioration in the vision of the right eye, and within ten months the eye was blind. There were no further symptoms, and the vision of the left eye had remained unaltered. She had had occasional headaches for years, not worse recently.

Clinical examination revealed a blind right eye, with a pupil fixed to direct light but reacting well consensually. The right optic disc was pale, with blurred edges, and the upper temporal vessels were sheathed. The left fundus was normal, the visual field full to 3/2000, and the visual acuity 6/9 (J2 with glasses). Sense of smell was normal, and there was no exophthalmos. The rest of the examination of the nervous system was normal.

The cerebrospinal fluid was under a pressure of 140 mm., contained 60 mg.% of protein, and no cells. The Wassermann reaction was negative in both cerebrospinal fluid and blood. Radiographic examination of the skull was normal, but the right optic foramen was slightly larger than that on the left side. There was no evidence of erosion of the walls of the right optic foramen, and the radiologist considered it was within the limits of normality. Air pictures showed good filling of the ventricular system, including the pontine and chiasmatic basal cisterns, and there was no evidence of any filling defect in



FIG. 10.—Arteriogram in Case VI, showing "blush" outlining the position of the meningioma.

*CASE VII.—Meningioma of the sphenoid with unilateral optic atrophy and slight exophthalmos.*

Mrs. M. M., aged 70. This patient complained of gradual failure of vision in the left eye starting in April 1948, five months previously. She had noticed that the visual loss was chiefly in the lower part of the left visual field. During this period, too, she had had intermittent left frontal headaches, though not severe in character. Her general health had remained good, and there was nothing of note in the past history.

Examination in September 1948 revealed a visual acuity of 6/6 partly in the right eye, but with ability only to count fingers in the remaining field of the left eye. There was a defect in the lower part of the left visual field, including fixation, the remaining vision being confined to a crescentic area in the upper field (fig. 11). The left optic disc was slightly pale, with slight blurring of the disc edges. The left pupil reacted poorly to direct light, but well consensually. There was slight left-sided exophthalmos. Sense of smell was normal, and further examination of the nervous system revealed no abnormality. The blood-pressure was 210 mm. Hg systolic, and 110 diastolic. Radiography of the skull showed sclerosis of the lesser and greater wings of the sphenoid on the left side, with involvement of the optic foramen, almost certainly due to diffuse meningiomatous involvement of the bone (fig. 12).

No operation was undertaken.

Although the diagnosis was not proved by microscopy, there is little doubt that the visual loss, exophthalmos, and radiographic changes in the sphenoid are due to a meningioma, as several similar cases have been seen, some of them verified by operation.

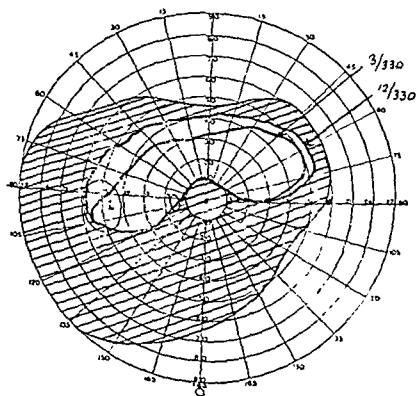


FIG. 11.—Visual field of Case VII.

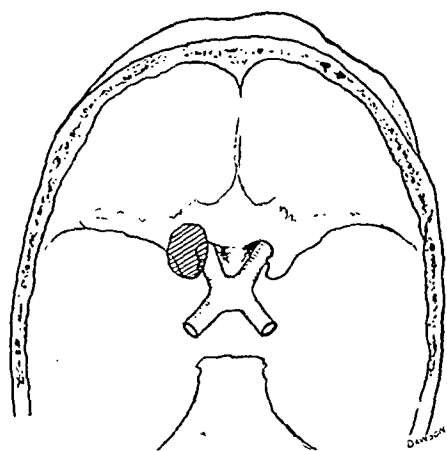


FIG. 9.—Diagram showing site of meningioma in Case V.

coughing or stooping. For about five months she had had frequent attacks in which she was seized with a feeling of terror, followed by a horrible smell or taste lasting a few seconds. The smell was always the same, and she likened it to a bonfire of burning garden hedges. Following this smell she lost the power of her legs and sank to the ground, but did not lose consciousness. Shortly before she was examined she noticed progressive visual failure in the right eye, the left eye being unaffected.

Examination in May 1948 revealed a cheerful, euphoric patient. The vision was reduced to 2/60 on the right side, and, to confrontation tests, there was a central scotoma in the right visual field. The right optic disc and fundus were normal. The left visual acuity was 6/9 and the left optic fundus and visual field were normal. The sense of smell was diminished on the right side. The rest of the nervous system was normal on examination.

A diagnosis was made of intracranial tumour, with direct pressure on the optic nerve, probably an olfactory groove meningioma.

Unfortunately the patient was not seen again until December 1948, when she had right-sided optic atrophy with no perception of light in the right eye. The right pupil was fixed to light, but reacted well consensually. The left eye was normal, and the field full.

Radiography of the skull showed increased bony density along the central part of the floor of the anterior fossa, more marked on the right side, consistent with the presence of an olfactory groove meningioma.

A right percutaneous arteriogram showed good filling of the internal carotid, anterior and middle cerebral arteries. There was a spherical "blush" above the floor of the right anterior fossa, about 6 cm. in diameter (fig. 10). There was a marked shift to the left of the right anterior cerebral artery in the A.P. view. The appearances suggested a large right olfactory groove meningioma.

Ventriculography showed that the septum was displaced about 2 cm. to the left of the mid-line. The anterior horns were much displaced posteriorly, and the third ventricle was not filled. The appearances suggested a large right subfrontal lesion.

Operation was performed on December 23, 1948, by Mr. McKissock. A right frontal bone flap was elevated, and the right frontal lobe amputated. A large ovoid meningioma occupied most of the anterior fossa on the right side, except for the anterior 2 cm. The tumour had a wide attachment, about 2 cm. in length, to the floor of the anterior fossa in the region of the olfactory groove. The tumour was completely removed, and weighed 59 grammes (5.5 × 4.5 × 4 cm.). On histological examination it proved to be a meningioma.

The post-operative course was uneventful, and there was some return of vision (perception of light only) in the lower nasal field of the right eye.

On April 13, 1949, nearly four months after operation, the patient felt very well indeed. There was some return of vision in the periphery of the right nasal field, where she could count fingers. The right optic disc was pale and there was right-sided anosmia.

(fig. 9). The medial aspect of the tumour was extending over and pressing on the right optic nerve. The optic nerve was freed and the tumour completely removed. The area of attachment to the anterior clinoid process was diathermized. Bleeding was minimal and the patient stood the operation well. Microscopy of the tumour proved it to be a meningioma.

Return of vision ensued with surprising rapidity, so that within a few days the patient could read with the right eye. On June 19, 1947, nearly three weeks after operation, visual acuity was 6/9 in the right eye, and the right visual field showed a defect in the lower temporal field (fig. 8).

*CASE VI.—Meningioma of the olfactory groove with unilateral optic atrophy and central scotoma.*

Mrs. E. M., aged 46. For eighteen months before examination the patient had had severe vertical headaches, worse on coughing or stooping. For about five months she had had frequent attacks in which she was seized with a feeling of terror, followed by a horrible smell or taste lasting a few seconds. The smell was always the same, and she likened it to a bonfire of burning garden hedges. Following this smell she lost the power of her legs and sank to the ground, but did not lose consciousness. Shortly before she was examined she noticed progressive visual failure in the right eye, the left eye being unaffected.

Examination in May 1948 revealed a cheerful, euphoric patient. The vision was reduced to 2/60 on the right side, and, to confrontation tests, there was a central scotoma in the right visual field. The right optic disc and fundus were normal. The left visual acuity was 6/9 and the left optic fundus and visual field were normal. The sense of smell was diminished on the right side. The rest of the nervous system was normal on examination.

A diagnosis was made of intracranial tumour, with direct pressure on the optic nerve, probably an olfactory groove meningioma.

Unfortunately the patient was not seen again until December 1948, when she had right-sided optic atrophy with no perception of light in the right eye. The right pupil was fixed to light, but reacted well consensually. The left eye was normal, and the field full.

Radiography of the skull showed increased bony density along the central part of the floor of the anterior fossa, more marked on the right side, consistent with the presence of an olfactory groove meningioma.

A right percutaneous arteriogram showed good filling of the internal carotid, anterior and middle cerebral arteries. There was a spherical "blush" above the floor of the right anterior fossa, about 6 cm. in diameter (fig. 10). There was a marked shift to the left of the right anterior cerebral artery in the A.P. view. The appearances suggested a large right olfactory groove meningioma.

Ventriculography showed that the septum was displaced about 2 cm. to the left of the mid-line. The anterior horns were much displaced posteriorly, and the third ventricle was not filled. The appearances suggested a large right subfrontal lesion.

Operation was performed on December 23, 1948, by Mr. McKissock. A right frontal bone flap was elevated, and the right frontal lobe amputated. A large ovoid meningioma occupied most of the anterior fossa on the right side, except for the anterior 2 cm. The tumour had a wide attachment, about 2 cm. in length, to the floor of the anterior fossa in the region of the olfactory groove. The tumour was completely removed, and weighed 59 grammes (5.5 × 4.5 × 4 cm.). On histological examination it proved to be a meningioma.

The post-operative course was uneventful, and there was some return of vision (perception of light only) in the lower nasal field of the right eye.

On April 13, 1949, nearly four months after operation, the patient felt very well indeed. There was some return of vision in the periphery of the right nasal field, where she could count fingers. The right optic disc was pale and there was right-sided anosmia.



FIG. 10.—Arteriogram in Case VI, showing "blush" outlining the position of the meningioma.

CASE VII.—*Meningioma of the sphenoid with unilateral optic atrophy and slight exophthalmos.*

Mrs. M. M., aged 70. This patient complained of gradual failure of vision in the left eye starting in April 1948, five months previously. She had noticed that the visual loss was chiefly in the lower part of the left visual field. During this period, too, she had had intermittent left frontal headaches, though not severe in character. Her general health had remained good, and there was nothing of note in the past history.

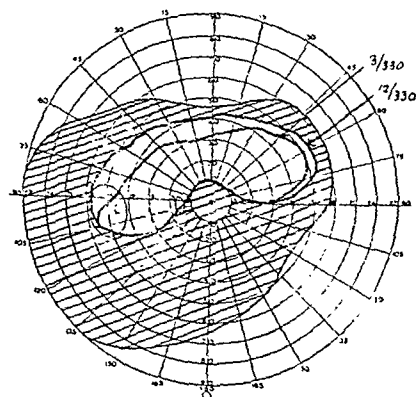


FIG. 11.—Visual field of Case VII.

Examination in September 1948 revealed a visual acuity of 6/6 partly in the right eye, but with ability only to count fingers in the remaining field of the left eye. There was a defect in the lower part of the left visual field, including fixation, the remaining vision being confined to a crescentic area in the upper field (fig. 11). The left optic disc was slightly pale, with slight blurring of the disc edges. The left pupil reacted poorly to direct light, but well consensually. There was slight left-sided exophthalmos. Sense of smell was normal, and further examination of the nervous system revealed no abnormality. The blood-pressure was 210 mm. Hg systolic, and 110 diastolic. Radiography of the skull showed sclerosis of the lesser and greater wings of the sphenoid on the left side, with involvement of the optic foramen, almost certainly due to diffuse meningiomatous involvement of the bone (fig. 12). No operation was undertaken.

Although the diagnosis was not proved by microscopy, there is little doubt that the visual loss, exophthalmos, and radiographic changes in the sphenoid are due to a meningioma, as several similar cases have been seen, some of them verified by operation.



FIG. 12.—Radiograph of Case VII, showing hyperostosis of sphenoid bone on the left side due to meningioma.

*CASE VIII.—Intracranial aneurysm with pressure on left optic nerve, with spontaneous improvement in vision.*

Mrs. H. A., aged 36. Early in 1946, about two years before she was first examined, the patient suddenly developed severe left frontal headache and pain in the left eye, associated with an "influenzal cold" and fever. The fever subsided after a few days, but the headache persisted for about two or three weeks. Soon after this, the patient noticed a gradual dimming of the vision of the left eye, which progressed for some months. She noticed loss of central vision of the left eye, but she could see clearly round the edges. This loss of vision remained almost stationary for about a year, but five months before she was examined the vision in the left eye rapidly deteriorated, so that she could discern only the general shape of large objects. Her general health remained good and there were no other symptoms of note.

In May 1946 it was noted that the vision of the left eye was 6/9, and that there was a sector-shaped scotoma running from the fixation point upwards and to the right in the left nasal field. In September 1947 the vision had fallen to 2/60 in the left eye, the left optic disc was pale, and there was a central scotomatous defect in the left field spreading to the periphery in the upper part of the field.

Examination in January 1948 showed a central scotoma in the left visual field and a slight defect in the upper right temporal field (fig. 13). The visual acuity was 6/6 (corrected) on the right side, but reduced to "counts fingers" at one foot on the left side. Both optic fundi showed evidence of myopia, with myopic crescents, and pallor of both optic discs more marked on the left side. The right optic disc was considered normal for the degree of myopia. The left pupil was slightly larger than that on the right side, and reacted poorly to direct light but well consensually. There was slight proptosis on the left side. The sense of smell was normal, and the rest of the central nervous system was normal on examination. There was no cephalic bruit, and the cardiovascular system was normal.

The cerebrospinal fluid was under a pressure of 120 mm., and of normal content, and the Wassermann reaction was negative in the blood and cerebrospinal fluid. Skiagrams of the skull and optic foramina showed no abnormality.



A myodil ventriculogram showed obliteration of the optic recess of the third ventricle, and deviation to the right of the bottom of the third ventricle, with slight elevation of the floor of the left anterior horn. These findings suggested an expanding lesion in the region of the left anterior clinoid process.

On January 12, 1948, operation was performed by Mr. Wylie McKissock, and a small left frontal bone flap was turned down. On elevation of the left frontal lobe, the left optic nerve was seen to be grossly widened from side to side, and displaced upwards and laterally by a large aneurysm, arising from either the left anterior cerebral, or anterior communicating artery. In view of the very soft wall of the aneurysm, no further operative procedure was undertaken, and the aneurysm was not needled.

On January 21, 1948, nine days after the intracranial exploration, left percutaneous arteriography was performed, which showed that the left anterior cerebral artery was elevated and pushed backwards, but no aneurysm was visualized. Five days later a right

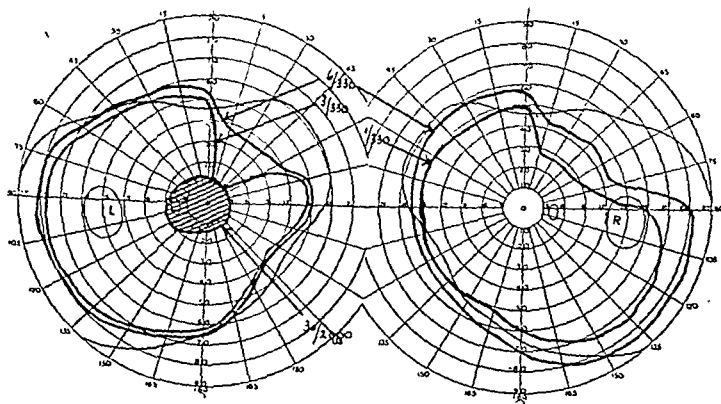


FIG. 13.—Visual fields of Case VIII (aneurysm).

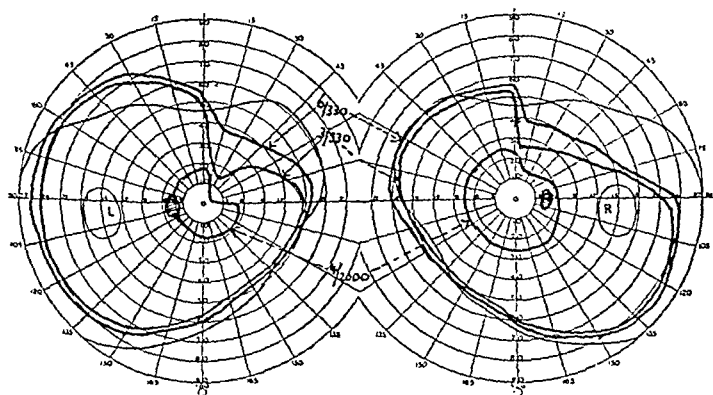


FIG. 14.—Visual fields of Case VIII, some months later, showing disappearance of central scotoma, but persistence of upper quadrantic homonymous defect.

percutaneous arteriography showed no definite abnormality, except that the anterior cerebral arteries did not fill.

The patient made an uninterrupted recovery from the operation, and in spite of the fact that no radical operative measures were taken, the vision in the left eye slowly improved. When seen on December 15, 1948, eleven months after the operation, the left visual acuity was 6/9 partly, and there was a partial right upper quadrantic homonymous defect, but no evidence of a central scotoma on the left side (fig. 14).

The improvement in the vision would appear to add further proof to the diagnosis of aneurysm.

CASE IX.—*Unilateral visual failure and central scotoma due to ? aneurysm.*

E. C., male, aged 45. Eight months previous to admission to hospital, the patient noticed gradual failure of vision of the left eye, with loss of central vision, the peripheral field being relatively intact. He had had occasional dull frontal headaches occurring about once a month for the previous four or five years, but there had been no increase in the headaches with the onset of visual failure. He had noticed no loss of sense of smell, and his general health had remained good. Past history and family history showed no relevant features.

Examination in January 1949 revealed slight pallor of both optic discs, more marked on the left side, with visual acuity of right 6/24 and left 1/60. There was a dense central scotoma on the left side, breaking through to the periphery in the lower nasal quadrant. The right field showed a slight defect in the lower temporal quadrant (fig. 15). The pupils

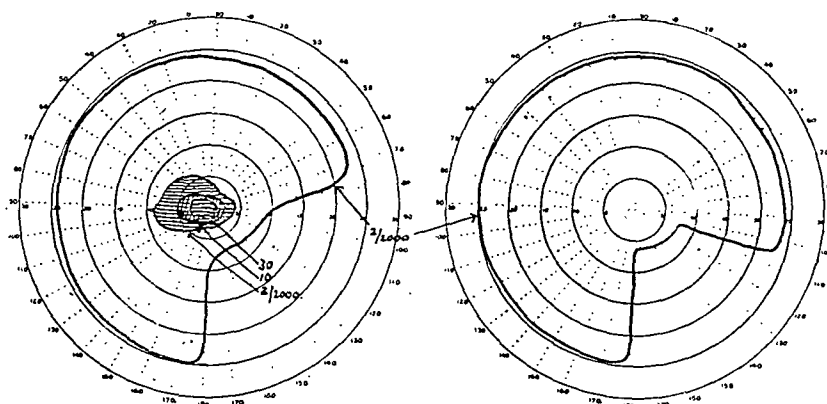


FIG. 15.—Visual fields of Case IX (? aneurysm).

reacted normally, ocular movements were full, and sense of smell was normal. The rest of the nervous system was normal on examination.

The cerebrospinal fluid was normal, the pressure being 140 mm., and the total protein 40 mg.%. Radiography of the skull showed no abnormality. Ventriculography showed a normal ventricular system, and a left percutaneous arteriography showed a normal arterial tree.

In spite of negative investigations it was considered justifiable to explore the region of the optic nerve and chiasm. On January 27, 1949, a right frontal approach (Mr. McKissock) revealed that the left optic nerve was elevated from below by an oval pinkish grey mass measuring 1 cm. in length. The tumour gave the impression of containing fluid, when it was palpated with a blunt hook. From its anterior extremity, and just medial to the optic nerve, an artery emerged and passed into the optic foramen medial to the nerve. It was considered that this tumour was probably an aneurysm. No radical treatment was undertaken.

After operation, the left-sided arteriogram was repeated, and again a normal arterial tree was demonstrated. Examination four months after the exploration showed virtually no change in the visual fields.

CASE X.—*Monocular blindness with cephalic bruit due to ? aneurysm.*

Mrs. A. J. S., aged 63. About Christmas 1948 this patient noticed a sudden onset of a beating noise in her head, which has persisted. For some weeks at this time she had right occipital headache, and for a few days there was diplopia. On March 21, 1949, nine days before she was examined, she noticed visual hallucinations in the right eye, of sudden onset, and lasting most of the day. Later the same day a grey mist appeared in the right temporal field and spread rapidly over the right eye, sparing the upper part of the field. The visual hallucinations were described as "blue lights like stars, with a red rim". Since the onset of the right eye, formed visual hallucinations occur on closing the right eye, "uncanny".

Examination on March 30, 1949, showed slight swelling of the right optic disc, which was also slightly pale, with a few hæmorrhages near the disc margin. Visual acuity was reduced to hand movements in the right eye, and the right visual field was reduced to a small island of intact vision in the upper temporal periphery (fig. 16). A loud systolic murmur was

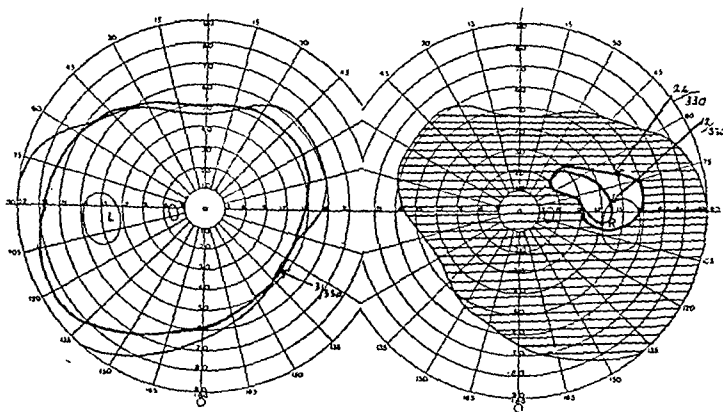


FIG. 16.—Visual fields of Case X.

audible all over the head, but was maximal on auscultation over the right eye, and was abolished by digital compression of the right common carotid artery in the neck. The right corneal reflex was reduced, but the other cranial nerves were normal. The rest of the nervous system was normal on examination, and the blood-pressure 140/90.

Radiographic examination of the skull was normal, and the cerebrospinal fluid showed no abnormality, the pressure being 120 mm. A right percutaneous carotid arteriogram showed fair filling of the common and internal carotid arteries, as well as the posterior cerebral and posterior communicating arteries, but no aneurysm was visible. There was, however, a sudden marked narrowing in the calibre of the internal carotid artery, as it passed through the cavernous sinus. This narrowing may be due to pressure of an aneurysm which does not fill with radiopaque substance.

On May 25, 1949, the right common carotid artery was ligated by Mr. Wylie McKissock, with no untoward effect. The cephalic bruit immediately ceased, but there was no improvement in the vision of the right eye.

Although the diagnosis is unproven in this case, the pathology is undoubtedly vascular, and probably aneurysmal.

#### CASE XI.—Glioma of optic nerves and chiasm presenting as thrombosis of central retinal vein.

J. B., male, aged 50. Four months before admission to hospital, the patient noticed progressive loss of vision of the right eye, so that it was blind within about two weeks. When seen at that time there was evidence of thrombosis of the central retinal vein, and the visual acuity was reduced to 6/36 in the right eye. During the next two months he developed severe pain in the eye, and three months after the onset the right eye was enucleated for secondary glaucoma. The vision in the left eye probably began to fail soon after the right eye became blind, and this failure progressed till admission to hospital.

For some weeks before admission the patient had slept a good deal, had become drowsy, and developed a huge appetite. Pain recurred behind the right orbit, and he became progressively tired and weak, and, more recently, confused.

On admission to hospital on April 6, 1948, the patient was slightly confused, drowsy, and inattentive. The right eye had been enucleated. The visual acuity in the remaining eye was 1/18, the left optic disc was slightly pale, and there was a hemianopia involving the left temporal field (fig. 17). There was slight spastic weakness of the right upper limb, and both plantar responses were extensor. Radiological examination of the skull and chest were negative.

CASE IX.—*Unilateral visual failure and central scotoma due to ? aneurysm.*

E. C., male, aged 45. Eight months previous to admission to hospital, the patient noticed gradual failure of vision of the left eye, with loss of central vision, the peripheral field being relatively intact. He had had occasional dull frontal headaches occurring about once a month for the previous four or five years, but there had been no increase in the headaches with the onset of visual failure. He had noticed no loss of sense of smell, and his general health had remained good. Past history and family history showed no relevant features.

Examination in January 1949 revealed slight pallor of both optic discs, more marked on the left side, with visual acuity of right 6/24 and left 1/60. There was a dense central scotoma on the left side, breaking through to the periphery in the lower nasal quadrant. The right field showed a slight defect in the lower temporal quadrant (fig. 15). The pupils

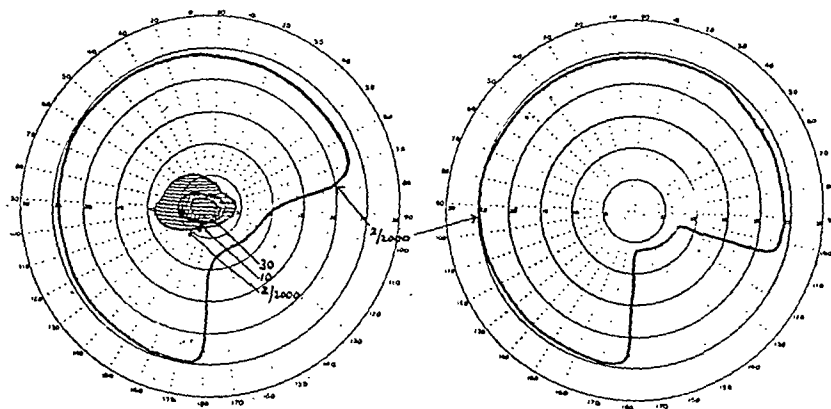


FIG. 15.—Visual fields of Case IX (? aneurysm).

reacted normally, ocular movements were full, and sense of smell was normal. The rest of the nervous system was normal on examination.

The cerebrospinal fluid was normal, the pressure being 140 mm., and the total protein 40 mg.%. Radiography of the skull showed no abnormality. Ventriculography showed a normal ventricular system, and a left percutaneous arteriography showed a normal arterial tree.

In spite of negative investigations it was considered justifiable to explore the region of the optic nerve and chiasm. On January 27, 1949, a right frontal approach (Mr. McKissock) revealed that the left optic nerve was elevated from below by an oval pinkish grey mass measuring 1 cm. in length. The tumour gave the impression of containing fluid, when it was palpated with a blunt hook. From its anterior extremity, and just medial to the optic nerve, an artery emerged and passed into the optic foramen medial to the nerve. It was considered that this tumour was probably an aneurysm. No radical treatment was undertaken.

After operation, the left-sided arteriogram was repeated, and again a normal arterial tree was demonstrated. Examination four months after the exploration showed virtually no change in the visual fields.

CASE X.—*Monocular blindness with cephalic bruit due to ? aneurysm.*

Mrs. A. J. S., aged 63. About Christmas 1948 this patient noticed a sudden onset of a beating noise in her head, which has persisted. For some weeks at this time she had right occipital headache, and for a few days there was diplopia. On March 21, 1949, nine days before she was examined, she noticed visual hallucinations in the right eye, of sudden onset, and lasting most of the day. Later the same day a grey mist appeared in the right temporal field and spread rapidly over the right eye, sparing the upper part of the field. The visual hallucinations were described as "blue lights like stars, with a red rim". Since the onset of blindness of the right eye, formed visual hallucinations occur on closing the right eye, "people waving things, most uncanny".

## Section of Medicine

President—Sir ADOLPHE ABRAHAMS, O.B.E., M.A., M.D., F.R.C.P.

[March 22, 1949]

### DISCUSSION: SPECIALIZATION—ITS VALUE AND ABUSE

Sir Robert Arthur Young: Specialization in Medicine is of very recent development. I was therefore surprised to find in the volume of the New Century Dictionary published in 1919 the first of many definitions of the word "specialist":—"A medical practitioner or authority who devotes his attention to the study of a particular disease or a Class of Diseases." I prefer the more terse and slyly humorous definition which I have not been able to trace—"one who devotes more and more attention to less and less". In justification of my statement that specialization in medicine is a comparatively recent development I recall that when I started my clinical work as a student there were a few special hospitals, notably those for diseases of the eye, the chest, nose and throat, the skin and the nervous system, also for diseases of women and for mental and venereal disease, but even these were for the most part staffed by men and women on the staffs of the general hospitals. Even in 1891, the *Lancet* (ii, 774) in a leading article states: "We are opposed to the Specialisation of Hospitals" and quotes with approval an Address by Dr. (afterwards Sir James) Goodhart, one of the wisest general physicians of his generation, in which he objects to the word Pædiatrics and deprecates most strongly regarding Diseases of Children as a speciality, though he was giving his Address before the Section of Diseases of Children at the British Medical Association and was himself a pioneer in that branch of medicine.

The chief arguments adduced against specialization were the tendency to run in grooves and to go to extremes, but the main objection was the failure to regard the human organism as a whole. Brought up medically as I was when such opinions were generally held, it is not surprising that my first reaction to the starting of Special Departments in my own Hospital was one of opposition. I soon realized, however, that they were inevitable and I recognize that their results have been in the main beneficent and to the public advantage.

The chief factors in the remarkably rapid advance of specialism in recent years are:

(1) The development and exploitation of instruments and instrumental methods in investigation and treatment. It seems almost incredible to read that when Sir James Paget was a first-year student and observed *Trichina spiralis* in human muscle, he had to borrow a microscope from a botanist to study them. The clinical laboratory is a development well within my own memory. In my student days practically the only routine laboratory investigations carried out were staining for tubercle bacilli and urinary tests, with an occasional red blood cell count and hæmoglobin estimation. Ehrlich's pioneer researches on the staining reactions of the leucocytes paved the way for the modern study of blood diseases. This, with the rise of bacteriology, made the clinical laboratory a necessity. It seems difficult now to realize how much physicians of that day had to depend on their senses and how large the classical sequence of inspection, palpation, percussion and auscultation loomed in our instruction. One unfortunate result of specialization is that we are liable to neglect or cut short our direct observation of the patient and appeal at once to laboratory or instrumental aids.

A very important and early addition to direct illumination of diseased areas was the invention of the laryngoscope in 1855 by Manuel Garcia, not a doctor, but a teacher of singing. At the present time we have multiple 'scopes for every orifice and where none exists we explore closed cavities through artificial openings. We expose the secrets of the bone-marrow by means of a drill, and the cavities of the heart with a cardiac catheter.

(2) Another factor in advancing specialization has been the ample gifts of science as applied to medicine—notably physiology, pathology, chemistry, especially biochemistry, and now biophysics, with its rich promise in the use of isotopes.

It is difficult now to imagine diagnosis of some conditions without X-rays. The develop-

On April 30, 1948, a right frontal lobectomy was performed by Mr. Harvey Jackson, and a tumour was seen involving both optic nerves, but no radical treatment was undertaken. The patient died two days later.

Autopsy revealed that both optic nerves were about one and a half times their normal size at the optic foramina. The left nerve gradually tapered in the orbit to normal size. The optic chiasm was greatly swollen, indefinite in outline, and incorporated in a plum-coloured thickening, which involved it and the infundibular region of the floor of the third

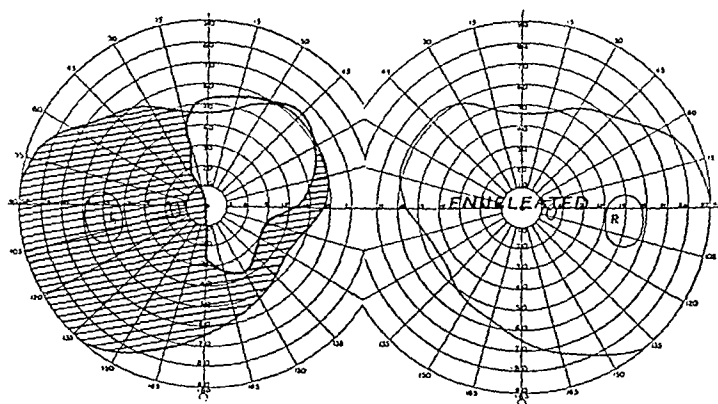


FIG. 17.—Visual fields of Case XI.

ventricle. The left optic tract was swollen for its first centimetre, and the left cerebral peduncle was one-third larger than the right. On section the chiasm and hypothalamus were occupied by a pale firm tumour, which spread to involve the cerebral peduncle and pons, and right lateral ventricle. Histological examination showed the tumour to be a glioma (glioblastoma multiforme).

I am indebted to my neurosurgical colleagues Mr. Harvey Jackson and Mr. Wylie McKissock for operative details in these cases, to Dr. Helen Dimsdale and Mr. Valentine Logue for the details and drawings of Case I, to Dr. William Blackwood for the autopsy report on Case XI, and to Dr. Hugh Davies and Dr. J. W. D. Bull for arteriographic and radiological investigations.

#### REFERENCES

- CUSHING, H., and EISENHARDT, L. (1938) Meningiomas. Springfield and Baltimore.  
 JEFFERSON, G. (1937) *Brain*, **60**, 444.  
 — (1945) *Trans. Ophthalm. Soc. U.K.*, **65**, 262.  
 MCKENDREE, C. A., and DOSHAY, L. J. (1936) *Bull. N.Y. Neur. Inst.*, **5**, 223.  
 MOONEY, A. J., and MCCONNELL, A. A. (1949) *J. Neurol., Neuro-Surg., Psychiat.*, **12**, 205.  
 MOORE, R. F. (1925) *Medical Ophthalmology*. London, p. 92.  
 SCHLEZINGER, N. S., ALPERS, B. J., and WEISS, B. P. (1946) *Arch. Ophthalm.*, **35**, 624.  
 SUNDERLAND, S. (1948) *J. Neurol., Neuro-Surg., Psychiat.*, **11**, 243.  
 TRAQUAIR, H. M. (1946) *Introduction to Clinical Perimetry*. London, p. 193.

Mr. Eugene Wolff said that he had long been puzzled as to why the disc became white after division or compression of the optic nerve. Also he had found no explanation in the literature. He suggested the following reason.

The optic nerve being part of the central nervous system does not, as is well known, obey the Wallerian laws of degeneration. There is in fact degeneration centrally and peripherally. The disappearance of the nerve fibres is followed by gliosis. This new-formed glial tissue then contracts and obliterates the capillaries of the nerve-head. And it is the disappearance of the capillaries which is essentially responsible for the white disc.

## Section of Medicine

President—Sir ADOLPHE ABRAHAMS, O.B.E., M.A., M.D., F.R.C.P.

[March 22, 1949]

### DISCUSSION: SPECIALIZATION—ITS VALUE AND ABUSE

Sir Robert Arthur Young: Specialization in Medicine is of very recent development. I was therefore surprised to find in the volume of the New Century Dictionary published in 1919 the first of many definitions of the word "specialist":—"A medical practitioner or authority who devotes his attention to the study of a particular disease or a Class of Diseases." I prefer the more terse and slyly humorous definition which I have not been able to trace—"one who devotes more and more attention to less and less". In justification of my statement that specialization in medicine is a comparatively recent development I recall that when I started my clinical work as a student there were a few special hospitals, notably those for diseases of the eye, the chest, nose and throat, the skin and the nervous system, also for diseases of women and for mental and venereal disease, but even these were for the most part staffed by men and women on the staffs of the general hospitals. Even in 1891, the *Lancet* (ii, 774) in a leading article states: "We are opposed to the Specialisation of Hospitals" and quotes with approval an Address by Dr. (afterwards Sir James) Goodhart, one of the wisest general physicians of his generation, in which he objects to the word Pædiatrics and deprecates most strongly regarding Diseases of Children as a speciality, though he was giving his Address before the Section of Diseases of Children at the British Medical Association and was himself a pioneer in that branch of medicine.

The chief arguments adduced against specialization were the tendency to run in grooves and to go to extremes, but the main objection was the failure to regard the human organism as a whole. Brought up medically as I was when such opinions were generally held, it is not surprising that my first reaction to the starting of Special Departments in my own Hospital was one of opposition. I soon realized, however, that they were inevitable and I recognize that their results have been in the main beneficent and to the public advantage.

The chief factors in the remarkably rapid advance of specialism in recent years are: (1) The development and exploitation of instruments and instrumental methods in investigation and treatment. It seems almost incredible to read that when Sir James Paget was a first-year student and observed *Trichina spiralis* in human muscle, he had to borrow a microscope from a botanist to study them. The clinical laboratory is a development well within my own memory. In my student days practically the only routine laboratory investigations carried out were staining for tubercle bacilli and urinary tests, with an occasional red blood cell count and hæmoglobin estimation. Ehrlich's pioneer researches on the staining reactions of the leucocytes paved the way for the modern study of blood diseases. This, with the rise of bacteriology, made the clinical laboratory a necessity. It seems difficult now to realize how much physicians of that day had to depend on their senses and how large the classical sequence of inspection, palpation, percussion and auscultation loomed in our instruction. One unfortunate result of specialization is that we are liable to neglect or cut short our direct observation of the patient and appeal at once to laboratory or instrumental aids.

A very important and early addition to direct illumination of diseased areas was the invention of the laryngoscope in 1855 by Manuel Garcia, not a doctor, but a teacher of singing. At the present time we have multiple scopes for every orifice and where none exists we explore closed cavities through artificial openings. We expose the secrets of the bone-marrow by means of a drill, and the cavities of the heart with a cardiac catheter.

(2) Another factor in advancing specialization has been the ample gifts of science as applied to medicine—notably physiology, pathology, chemistry, especially biochemistry, and now biophysics, with its rich promise in the use of isotopes.

It is difficult now to imagine diagnosis of some conditions without X-rays. The develop-

ment of radiology as a speciality and its recent fission into the two specialities of radio-diagnosis and radiotherapy afford a striking example of the increasing complexity of specialist work.

(3) The third influence in fostering specialization has been the public demand for special knowledge and skill. This is often fostered prematurely by the lay Press, with the best intentions, but with unfortunate results.

I do not like the word "abuse" in either of its pronunciations or meanings. The only abuses of specialism that I can see are its employment as a cloak for the crank, or as a spotlight for the quack, but after all such are only pseudospecialists.

I regard as a misuse of the benefits of specialization a direct approach by the patient or his friends to the specialist, and a too-ready acquiescence in this approach by the specialist without the cognizance and approval of the physician or general practitioner in charge. The profession of the Law manages these matters in some ways better than we do, as direct approach to the specialist is not permitted, and normally is arranged through the solicitor.

In this connexion, I feel great care will be necessary in the organization of the Health Centres under the new Health Act. They should afford what most of us have earnestly desired for years—namely that all necessary investigations and treatments should be available for all patients and not limited by capacity to pay. The routine use of such centres must be controlled, and it should be the general practitioner in charge of the patient who should advise what investigations are necessary.

Being old-fashioned, I fear that specialization is having, or is likely to have, several disadvantages or unfortunate results in medical education and general practice. I fear we are witnessing the passing of the general physician. The student in all stages of his curriculum is taught by specialists, the best of whom are enthusiasts. Even in the general wards there is a tendency for cases to be directed or to gravitate to the physician or surgeon specially interested in the particular organ or system involved. It is, of course, impossible for any one man nowadays to acquire a general conspectus of disease, but I still think the methods of the older physicians should not be cast aside. I am still of opinion that time taken in eliciting the history of the patient and in a routine examination is often time saved in determining what specialized help, if any, is necessary. It was instruction on these lines by the general physicians which produced the flower of our profession—the general practitioner, who was the trusted guide, philosopher and friend of most of the families under his care, and whose advice was sought on many matters outside the sphere of medicine. At present the general practitioner is involved in a vortex of regulations, forms, certificates and reports. When these have settled and he is free to carry out his own legitimate work, he will wish to become, as of old, free to be the trusted, unhurried and unharried adviser of his patients, and free to use the Health Centres, when they have been established, for the best help of his patients.

I anticipate that, when the present pendulum swing of change has swung to its limit, a Minister of Health will send an exhortation, direction, or special instruction to the Medical Schools to produce doctors of the old type, with their eyes and interest on the general make-up of their patients and not on special departments of his economy. We must not be slaves of the lamp, the laboratory or of any mechanism, though always using them to the utmost when they can help. We are concerned with a sick or suffering human being and should study him first at the bedside, or in the consulting room. We must appeal for specialist aid whenever it is likely to be helpful, either in diagnosis or treatment, but we have a duty to protect him from the myopic outlook of the ultra-specialist, and the wiles of the quack.

**Mr. A. Dickson Wright:** There is no doubt that the specialists are greatly on the increase and as they filch more and more departments from the general surgeon and physician, these rather lose in stature and status, much as the general practitioner is losing status fast as a result of recent changes in the character of his work.

Yet the great strength of British medicine in the past lay in a very high standard of general practice so that patients became coupled to their home doctor. They did not forage alone among the consultants, but always in company with the family doctor who knew the second opinions which would help his patient most and who, at the same time, supplied valuable information on the patient's past and background. How different in other countries like America where the unfortunate patient drifts about among the specialists like a ship without a rudder! Perhaps this system is inevitable in the mixed restless population of America constantly fed with health articles and propaganda in its lay journals. Perhaps in this country a different form of medicine is more suited to our more phlegmatic and less hypochondriacal population.

Recent influxes of population from abroad have made us conscious of a pressure for more investigations and more laboratory work from these patients and their doctors and there seems to be a drift in this direction, especially as the State is fostering this extravagant form of medicine.



The newly qualified doctor very often has had his eye on a speciality even before he qualified and starts immediately on his course after qualification. He knows that if he wastes time in acquiring a good grounding in general medicine or surgery, he will be suspected of dallying and if he persists in this dallying after appointment to a post in a narrow speciality, he will be suspect by all, by co-specialists for lack of purity, by the general clinician for wandering out of his domain and by the patient, for failing to provide the undivided attention his special complaint requires.

In the teaching hospitals the narrow specialist was in a very happy position; the examining boards did not contain people such as he so the students left him alone. He thus escaped all the arduous of teaching, while, at the same time, he had all the advantages of a teaching hospital appointment. The teaching of the students was left to the more pedestrian general surgeons and physicians.

There are a few signs now of the specialist to-day expanding his field and imperceptibly melting back into the general sphere, often because there is not a livelihood in a narrow and unremunerative speciality.

Then again there are signs of the specialist becoming bored with his narrow monotony. The throat surgeon is extending his activities to the neck and dealing with pharyngeal out-pouchings such as the thyroid or the lymph glands that drain the throat and pharynx. The gynaecologist takes on the breast because it is linked to the sexual armamentarium, the thoracic surgeon takes note of the œsophagus and is soon dipping below the diaphragm to secure portions of intestine or stomach to take its place. The predatory tendencies of the orthopaedic surgeons are well known and their field is being increased at an alarming rate. It would seem that a narrow speciality, once established with its special societies and degrees, soon grows restless and in looking for new fields becomes more and more general.

One other evil of specialization is the danger of over-treatment. The patient newly arrived has to be convinced that he is dealing with a real specialist and is cystoscoped there and then, often without investigation as to the sterility of his urine. Or gastroscopy may be carried out quite unnecessarily, or all the elaborate ritual of the cardiologist put in train without enough clinical evidence to justify it. These examinations are costly, but, more important, they are sometimes dangerous and the patient gets more than he deserves. For instance, I have known very severe consequences follow a needless cystoscopy. In other fields methods are applied to patients which are of research quality and not justified for routine cases, e.g. cardiac catheterization and liver punctures.

In conclusion, it is to be hoped that in the future our doctors will have a first-class cultural education before starting medicine and will have some experience of general practice before starting a consultant career and, if specializing, will have a good grounding in medicine or surgery before drifting into a small department of the same. It is to be hoped that some specialities will diminish, especially specialism by diseases; for instance, the specialist in cancer automatically makes himself a specialist in every organ of the body in which cancer is found and thus may steal a march upon his colleague who has specialised with great industry in an organ or a system.

Sir Henry Cohen: As soon as the corpus of knowledge outgrew the capacity of any one man's intellectual embrace then specialization with its consequent narrowing of outlook became inevitable. Convenience, purpose, common features, interest and experience were the factors which shaped the emerging fields of the sciences and the practical arts, and it was natural that medicine, with its triple goal of aiming at the highest standards of health, preventing disease, and alleviating and curing illness, should develop as one of the major, though special, branches of knowledge. But no clear-cut boundaries between medicine and other arts and sciences could be drawn and in the overlapping fields were to be found some of its most fruitful growths. Big discoveries in medicine have often been the result of "bridge-work", as Burdon-Sanderson was so fond of saying.

When, therefore, we come to consider the value and abuse of specialization in medicine we must recognize the major fields of medicine itself. This deeper analysis of our problem demands that we should relate it to medical research, medical teaching, and medical practice.

The present tendency in research is undoubtedly towards a narrowing of any one investigator's interests. In bacteriology a man might devote his whole life to the streptococci, or to the viruses; in biochemistry one hormone or one vitamin might dominate the whole of a team's energies. Specialization in research is perhaps inevitable because of the intricacy of many of the modern instruments of research, e.g. the electron microscope, special methods of histopathology and bacterial culture or spectroscopic analysis. But it has led to workers in one field often being ignorant of advancing knowledge in another, and in medicine to a conflict between the clinical and laboratory researcher. It is perhaps not without interest to recall that many of the great figures of the past were able to illuminate many fields of medical research.

It is in teaching that the baneful effects of over-specialization in practice have become so evident. Instead of our textbooks being imbued with a general philosophy of medicine, they are accretions of monographs written by different authors in which the principles of medicine which should pervade all undergraduate teaching are obscured or lost. These textbooks resemble patchwork quilts instead of being like a tapestry whose design is clearly evident. Again, the population of our teaching hospitals has become more specialized and because of the narrow interests of those in charge the wards are too often filled with cases similar in type, e.g. genito-urinary surgery, neurology, or cardiology, so that the student during his clerking sees, for example, a surfeit of rare heart conditions instead of a wide selection of the commoner manifestations of disease. He thus fails to acquire that experience which shows him that the methods of history taking and of clinical examination are the same whatever the site and nature of disease. Thus specialization in practice has led to defects of undergraduate medical teaching, which have too often prevented the undergraduate acquiring a general philosophy of medicine.

The practice of medicine has witnessed in the past fifty years an outcrop of an almost uncontrollable spate of specialities and they continue to appear. Some are based on age periods, e.g. paediatrics and geriatrics. Others have essentially an anatomical basis, e.g. neurology, cardiology, gynaecology, dermatology, ophthalmology and orthopaedics, whilst others are based on therapeutic measures, e.g. physiotherapy, radiotherapy, homœopathy. Still other specialities lie essentially in the diagnostic field, e.g. radiodiagnosis and clinical pathology; the latter is now being broken up into such branches as hæmatology and immunology. Occasionally the cause of disease defines a speciality, e.g. tuberculosis, allergy, and venereal disease, and in yet other instances a single manifestation of disease, e.g. diabetes mellitus or asthma, may be deemed adequate to justify the label of a specialist. Psychiatry and the various branches of surgery overlap some of these fields.

How far specialization in practice is justified depends to a considerable degree on the conception one has of the machinery of medical practice. Mine is relatively simple. I emphasize the place of the general practitioner or family doctor, who should be the first person to see his patient whatever the complaint. With perhaps 90% of illness, the G.P. can deal without further help. He might, however, need the services of a radiologist (e.g. to exclude a fractured bone), or of a clinical pathologist (e.g. to carry out a detailed blood-count, glucose tolerance test, or W.R.). But with the information thus provided the G.P. should be quite competent to manage his patient's disability and deal with it in relation to such social factors as home environment, personal relationships, work, &c., in a way in which no specialist can. Moreover, the G.P. might be in need of a specialist's help in regard to such treatment as surgery, physiotherapy, or radiotherapy. All these specialists have an important part to play in the practice of medicine; their skill in craftsmanship should increase with their experience. There will remain, however, some cases with which the general practitioner is unable to deal because he cannot define the problem which the patient presents within the narrow confines of a single speciality. His patient complains of backache; should she be sent to an orthopaedist, a gynaecologist, a rheumatologist, a neurologist, or any other compartmentalist whose especial competence might lead him to make a diagnosis in his field, but who otherwise is too often only justified in saying "There is nothing wrong in my department"? There surely must be available for these problems men of wide knowledge, wisdom and experience to whom the G.P. can refer his difficulties and these men—the true consultant physicians (not specialists!)—should take the whole field of practical medicine as their province and be familiar not with the techniques of, for example, laboratory tests or surgical operations, but with their purpose, value and limitation. Though the training and outlook of such physicians must be general they may well find a special interest in such branches as neurology or cardiology. We are in real danger of losing this type of general physician and I would plead that both for teaching and for practice his high place in the hierarchy of medicine should be assured.

What are the dangers of practice in a special field? The first and perhaps the most important is that the specialist is too often biased in relating pathological findings in his special field to the patient's disability. The presence of gall-stones does not mean that they are responsible for the patient's substernal pain; osteoarthritic changes in the cervical spine do not necessarily underlie the pains radiating down the left arm. How often have so-called uterine displacements been corrected without benefit to the patient so treated? Alleged focal sepsis in tonsils and teeth and the crimes committed in its name are one of the darkest chapters in the history of medical thought. Secondly, the practice of medicine demands that man be treated as a "whole". A cerebral tumour referred to a neurologist might well be secondary to a bronchial carcinoma which is giving but slight evidence of its presence, or to a hypernephroma. Cardiovascular disease might first manifest itself as a neurological lesion. Bone disease might be the expression of a metabolic defect or of renal inadequacy. To what specialities do such commonly combined lesions belong? There is yet a third and,

I hope, subconscious danger of specialization for the surgeon who has become a slave to a technique and who takes great pride in its performance. Too often, for him, the feasibility of an operation is an adequate indication for its performance.

What then in view of our discussion might be regarded as justifiable specialities? It is clear that those which involve technical skill at its highest level for both diagnostic and therapeutic purposes can be justified on the grounds that the narrower the field and the longer one's experience in its techniques and practice the better will be the performance. But it is paramount that such special procedures must be related to the needs of the "whole" man by his G.P. or a consultant physician. Man is greater than the sum of his parts. Secondly, where in any branch of medicine, e.g. pædiatrics or geriatrics, there is, to use Smuts' phrase, the "holistic" outlook, there the speciality is justifiable. Above all we must beware of becoming the slaves of instruments. "It takes a man and not a machine to understand a man."

Finally, however, I would reiterate my plea for the true consultant general physician, the "wise man" of medicine. I hope that this will not be regarded as a piece of special pleading. Both in teaching and practice, if the best is to be achieved, we need men of high intellectual gifts who are prepared to spend sufficient time in acquiring a wide experience over the whole field of diagnostic and therapeutic medicine so that when they are confronted by a difficult problem they can not only bring to bear on it the knowledge and wisdom they have acquired, but also appreciate whence they may seek help and the significance of that help in solving the problem presented by their patient.

[April 26, 1949]

## DISCUSSION ON NON-TUBERCULOUS CONDITIONS REVEALED BY MASS RADIOGRAPHY

**Dr. James Maxwell:** The great majority of discussions which have been held upon the various aspects of mass radiography have centred upon the problem of tuberculosis and, indeed, it was for the detection of early tuberculous disease that mass radiography was first introduced in this country. This aspect of the subject has been fully ventilated on many occasions, but the other side of the diagnostic picture has never been presented in detail. The object of the present discussion is presumably to restore the balance, and therefore it is confined to those cases which have hitherto been kept in the background. In this way it should be possible to obtain some sort of perspective, and at the same time to widen our horizon, as we realize that miniature mass radiography can be used to tackle the fundamental problems of disease in the chest, both of the respiratory system and also of the heart.

The opportunity for clinical research which is afforded by a mass X-ray unit is immense and a broad outlook is necessary if the best results are to be obtained. The clinical material differs entirely from that which is commonly encountered in an out-patient department, or even in a chest clinic, for the great majority do not complain of any symptoms and some are even inclined to resent the implication that there is anything wrong with them. An entirely different approach is necessary in dealing with patients of this type. It must be remembered that most of them are volunteers and that, being free from symptoms, they are less willing than the average out-patient to undergo investigations which may be troublesome from their point of view, and for which they do not see the need. One frequently has to exercise the greatest patience in persuading the patient that further investigation of the condition is in his own interest, and a tactful and sympathetic approach is even more necessary in these cases than it is when one is dealing with those who realize that they are sick and who seek help on that account.

There is no need for a full statistical analysis of the cases which have been surveyed since mass radiography began and in order to achieve our object it is sufficient to quote a very few figures. In the years 1946, 1947 and 1948 the Ministry of Health Mass Radiography Unit has detected a total of 3,423 abnormalities which were considered to need clinical investigation. These can be simply split up as follows:

|                               | Cases |
|-------------------------------|-------|
| Active tuberculosis .. ..     | 683   |
| Inactive tuberculosis .. ..   | 1,515 |
| Non-tuberculous conditions .. | 1,225 |

It will be seen that the greatest proportion of cases which are detected on a mass X-ray unit are found to fall into the group of inactive tuberculosis, but non-tuberculous conditions also form a very considerable group, comprising 35% of the total cases sent up for examination.

In this discussion it is proposed to concentrate on certain groups of cases, and in the first place to consider the group of acute lung inflammations which are found in ambulant cases.

*Pneumonitis.*—The term "pneumonitis" is here used to indicate those cases of pulmonary consolidation of greater or lesser degree which occur in patients who are not feeling really ill, although many of them admit to a recent attack of "influenza" or, perhaps, a rather severe cold. The term "pneumonitis" is preferable to some of the alternatives introduced to describe the condition, for it simply indicates that there is an inflammation of the lung and it does not commit us to any opinion on pathology, such as is implied in the term "virus pneumonia" which is sometimes applied to this type of case. The diagnostic problem may be very considerable, for the patient is not particularly ill and a very similar X-ray appearance can be presented by early tuberculosis and by early carcinoma. A history of a recent acute respiratory infection may be regarded as a fairly strong indication that the condition is likely to be pneumonitis, but the possibility that the X-ray appearance may represent something more serious must never be overlooked. Of course, the sputum should be examined for tubercle bacilli in all cases, and the other essential feature in diagnosis is to arrange for a comparative series of X-ray films in order to watch the progress of the condition. Most of the areas of acute consolidation which are correctly labelled "pneumonitis" are found to resolve between three and eight weeks, whereas the more serious conditions would be unlikely to show any regressive changes during that period. Unfortunately a similar smudge on the X-ray film might represent an early carcinoma, and this would be quite beyond the range of the bronchoscope in most cases, so that a certain amount of clinical flair is necessary in sorting out the cases and in selecting the occasional carcinoma for further action. The only way in which this condition can be adequately dealt with is by prompt operation, and the selection of cases, when they are detected at such an early stage, seems to need a considerable clinical instinct in order to avoid the twin errors of exploration of an innocent condition and delay in operation upon early malignant disease.

We see so many of these cases of innocent pneumonitis that it is important that we should remember that even these may give rise to occasional complications. Bronchial obstruction frequently causes a small area of segmental collapse in the lung, and this again produces a picture which can simulate an early carcinoma very closely. These areas of inflammatory collapse are very transient as a rule, and serial X-ray films should demonstrate their nature. Another occasional complication of pneumonitis is the development of a lung abscess. The patient is sometimes quite unaware that any serious lung condition is present although, in other cases, there may have been some symptom such as hæmoptysis which would indicate that lung disease is present. The X-ray appearance of a recent simple lung abscess may closely resemble that of a tuberculous cavity, and mistakes in diagnosis are sometimes made, although a persistently negative sputum should be regarded as fairly conclusive evidence against tuberculosis. These cases are not common and it is noteworthy that they appear to be quite innocent and the abscess heals as a rule without any necessity for special treatment.

Mention may be made here of a small group of cases which have not been recognized very frequently in the past. The X-ray shows areas of patchy inflammation in both lungs and the patient may complain of very little in the way of symptoms. There may be a certain amount of cough and sputum, but the clinical appearance is rather that of chronic bronchitis than any more serious condition. Careful study of the X-ray film may reveal a widening of the mediastinal shadow but, in the slighter cases, a barium swallow is necessary in order to demonstrate the previously unsuspected presence of a mega-œsophagus. The inflammation in the lungs is a "spill-over" effect, and it is rather curious that the great majority of these patients do not complain of any particular difficulty in swallowing. In fact, the lesser grades of the condition may easily be overlooked on the plain X-ray film and the diagnosis may be missed unless the possibility is constantly kept in mind.

*Collapse of the lung.*—A common finding during the investigation of a large series of cases is the presence of small areas of segmental collapse. Mention has already been made of a group of cases in which the collapse is due to a transient bronchial obstruction with mucus or mucopus. However, similar areas of collapse are found in other cases in which there is a history of chest disease, such as pneumonia, in the past but there are no symptoms at present. There can be no doubt that previous lung inflammation can cause permanent collapse of small areas of the lung, and it is well-known that a transient mediastinal glandular enlargement may cause sufficient pressure on a bronchus to produce a similar effect. It is less well recognized that old chest injury may result in permanent collapse of a portion of the lung. In this connexion it may be forecast that we are likely to find such cases among those who have been subjected to blast effect during the recent war and, indeed, one such case was discovered in which the chest injury had occurred in 1917. These silent areas of collapse may be very suggestive of carcinoma, but the history of exposure to blast may be regarded

as reassuring. It is always better, however, to advise bronchoscopy in cases of this sort in order to exclude the presence of early malignant disease.

*Sarcoidosis.*—Although there are fairly numerous references in the literature to pulmonary sarcoidosis, the clinical picture of this disease is still very imperfectly understood. Mass radiography has revealed the existence of quite a large group of cases in which there is a miliary condition in the lungs, which superficially resembles chronic miliary tuberculosis, and yet which is not associated with any particular symptoms and which runs a benign course. The fully developed picture of sarcoidosis, with enlargement of glands, skin lesions and other manifestations, is not particularly difficult to recognize and it is possible to obtain histological confirmation of the diagnosis in some cases.

When the only abnormal finding is an odd X-ray appearance the diagnosis must remain a matter of speculation in most cases, and here again there is a need for serial X-rays followed up for many months or even years. It is difficult to make a firm diagnosis in many of these cases but a clinical picture is beginning to emerge in our minds as the result of our follow-up. The earliest phase appears to be a simple enlargement of the mediastinal glands. At this stage there is obviously a differential diagnosis from tuberculosis, lymphadenoma and some of the rarer conditions in which lymphatic glands are enlarged. All of the ordinary clinical tests are negative, and considerable significance must be attached in this connexion to a negative Mantoux test. In some cases we have been able to follow the development of the miliary phase of sarcoidosis from this enlargement of the glands, and the full-blown picture appears to be one of a healthy-looking patient, usually without physical signs in the chest, and with this odd X-ray appearance. The lesions are hardly so round or so uniformly distributed as they are in miliary tuberculosis. They are rather more irregular and sometimes there is an appearance almost suggestive of silicosis. The most curious feature of all is that these very extensive lung lesions may be found in a patient who is clinically perfectly well. A follow-up by means of serial X-rays has shown that a small proportion clear up in the course of one or two years, but in many cases there has been comparatively little change during a period of over three years' observation and the disease appears to be quiescent. In our survey we have not yet learnt anything more of the pathology or the prognosis of this condition, for there have been no fatalities and, in fact, no patient is worse at the end of this period and several have shown definite X-ray improvement.

*The diaphragm.*—Lesions of the diaphragm are not easy to detect on physical examination as a general rule; there are very often no distinctive symptoms and therefore an abnormality is almost certain to be overlooked unless X-ray screening or radiography are employed. Our survey has shown up a group of cases in which there appears to be a spontaneous paralysis of the diaphragm. There are no symptoms and, as a general rule, no physical signs to be detected, so that the lesion would have passed unrecognized in all of these cases unless they had been submitted to routine radiography. The great majority recovered within the course of a few months and it has been suggested that this spontaneous paralysis of one side of the diaphragm is the result of an extremely mild attack of poliomyelitis. While this may, in fact, be the explanation of these cases it seems strange that this very definite syndrome should occur as part of an infection which is essentially general in its incidence, and it seems more reasonable to suppose that the condition is in reality a neuritis of the phrenic nerve. The condition itself would seem to be more closely allied to Bell's palsy and some of the other states in which a single nerve is affected. It is difficult to see how we can obtain further evidence about the mechanism of the paralysis in these cases, for they are not ill and there is no justification for an elaborate investigation.

*Conclusion.*—This brief survey of some of the non-tuberculous conditions revealed by mass radiography indicates that this method of clinical observation can play a vital part in the detection of an early and treatable non-tuberculous disease. It is by far the best method which we have at our disposal for the study of symptomless chest conditions and it opens up a wide field of observation which may serve greatly to extend our knowledge of chest disease. The influence of mass radiography may well make itself felt throughout the whole field of thoracic medicine and our future progress is likely to be largely determined by the use to which we put this most valuable instrument of clinical investigation.

**Dr. Peter Kerley:** Mass radiography would appear to offer little scope for the detection and investigation of cardiovascular abnormalities but surprisingly enough it is yielding information of considerable value and interest. The total number of civilians examined between June 1945 and June 1948 was three millions. 80% were between the ages of 15 and 45 years and the remaining 20% between 45 and 65 years. The sexes were equally represented. These statistics have been broken down for tuberculosis and bronchial carcinoma but not for cardiovascular abnormalities. However, we have certain information from two samples from

In this discussion it is proposed to concentrate on certain groups of cases, and in the first place to consider the group of acute lung inflammations which are found in ambulant cases.

*Pneumonitis.*—The term “pneumonitis” is here used to indicate those cases of pulmonary consolidation of greater or lesser degree which occur in patients who are not feeling really ill, although many of them admit to a recent attack of “influenza” or, perhaps, a rather severe cold. The term “pneumonitis” is preferable to some of the alternatives introduced to describe the condition, for it simply indicates that there is an inflammation of the lung and it does not commit us to any opinion on pathology, such as is implied in the term “virus pneumonia” which is sometimes applied to this type of case. The diagnostic problem may be very considerable, for the patient is not particularly ill and a very similar X-ray appearance can be presented by early tuberculosis and by early carcinoma. A history of a recent acute respiratory infection may be regarded as a fairly strong indication that the condition is likely to be pneumonitis, but the possibility that the X-ray appearance may represent something more serious must never be overlooked. Of course, the sputum should be examined for tubercle bacilli in all cases, and the other essential feature in diagnosis is to arrange for a comparative series of X-ray films in order to watch the progress of the condition. Most of the areas of acute consolidation which are correctly labelled “pneumonitis” are found to resolve between three and eight weeks, whereas the more serious conditions would be unlikely to show any regressive changes during that period. Unfortunately a similar smudge on the X-ray film might represent an early carcinoma, and this would be quite beyond the range of the bronchoscope in most cases, so that a certain amount of clinical flair is necessary in sorting out the cases and in selecting the occasional carcinoma for further action. The only way in which this condition can be adequately dealt with is by prompt operation, and the selection of cases, when they are detected at such an early stage, seems to need a considerable clinical instinct in order to avoid the twin errors of exploration of an innocent condition and delay in operation upon early malignant disease.

We see so many of these cases of innocent pneumonitis that it is important that we should remember that even these may give rise to occasional complications. Bronchial obstruction frequently causes a small area of segmental collapse in the lung, and this again produces a picture which can simulate an early carcinoma very closely. These areas of inflammatory collapse are very transient as a rule, and serial X-ray films should demonstrate their nature. Another occasional complication of pneumonitis is the development of a lung abscess. The patient is sometimes quite unaware that any serious lung condition is present although, in other cases, there may have been some symptom such as hæmoptysis which would indicate that lung disease is present. The X-ray appearance of a recent simple lung abscess may closely resemble that of a tuberculous cavity, and mistakes in diagnosis are sometimes made, although a persistently negative sputum should be regarded as fairly conclusive evidence against tuberculosis. These cases are not common and it is noteworthy that they appear to be quite innocent and the abscess heals as a rule without any necessity for special treatment.

Mention may be made here of a small group of cases which have not been recognized very frequently in the past. The X-ray shows areas of patchy inflammation in both lungs and the patient may complain of very little in the way of symptoms. There may be a certain amount of cough and sputum, but the clinical appearance is rather that of chronic bronchitis than any more serious condition. Careful study of the X-ray film may reveal a widening of the mediastinal shadow but, in the slighter cases, a barium swallow is necessary in order to demonstrate the previously unsuspected presence of a mega-œsophagus. The inflammation in the lungs is a “spill-over” effect, and it is rather curious that the great majority of these patients do not complain of any particular difficulty in swallowing. In fact, the lesser grades of the condition may easily be overlooked on the plain X-ray film and the diagnosis may be missed unless the possibility is constantly kept in mind.

*Collapse of the lung.*—A common finding during the investigation of a large series of cases is the presence of small areas of segmental collapse. Mention has already been made of a group of cases in which the collapse is due to a transient bronchial obstruction with mucus or mucopus. However, similar areas of collapse are found in other cases in which there is a history of chest disease, such as pneumonia, in the past but there are no symptoms at present. There can be no doubt that previous lung inflammation can cause permanent collapse of small areas of the lung, and it is well-known that a transient mediastinal glandular enlargement may cause sufficient pressure on a bronchus to produce a similar effect. It is less well recognized that old chest injury may result in permanent collapse of a portion of the lung. In this connexion it may be forecast that we are likely to find such cases among those who have been subjected to blast effect during the recent war and, indeed, one such case was discovered in which the chest injury had occurred in 1917. These silent areas of collapse may be very suggestive of carcinoma, but the history of exposure to blast may be regarded

aneurysms of the great vessels, transposition of the coarcted aorta and even transposition of the ventricles. Because the tube is slightly angulated and a grid used in mass radiography, rib notching is probably easier to detect on a miniature film than on a routine large one.

#### OTHER VASCULAR ANOMALIES

The commonest vascular anomalies after coarctation are right-sided aorta and aberrant right subclavian artery. These anomalies are easily mistaken for non-vascular mediastinal tumours. The correct diagnosis can be made by giving a barium swallow, which shows reversal of the normal oesophageal impression with right-sided aorta and a spiral impression with aberrant right subclavian artery. If there is a short and tight ligamentum arteriosum the oesophagus is constricted in these cases and dysphagia may occur. 2 out of 18 cases had slight difficulty in swallowing.

Simple transposition of viscera has been recorded in 1 in 50,000 people. A few of the more complex transpositions with eccentric reversal of the ventricles and auricles have been seen. These were associated with marked abnormality of the intrapulmonary vessels. One boy with a large heart and signs indicating an interventricular defect had remarkable anomalies of his intrapulmonary vessels. His mother and two sisters had similar abnormal intrapulmonary vessels without cardiac abnormality.

Few cyanotics present themselves for mass radiography. We have no figures of the numbers found with a left-right shunt but interatrial defects are not uncommonly found and 9 cases of patent ductus arteriosus have been noted.

**Dr. Thomas Paxon:** In a discussion of non-tuberculous conditions revealed by mass radiography, intrathoracic neoplasms should have an important place. It is necessary to state how easy it is to detect on miniature films tumours such as neurofibromata in their early stages. As 95% of miniature films prove to be normal any abnormalities appear unusually obvious.

Bronchial carcinoma is a very serious problem. The table shows the death-rate from carcinoma of the stomach and duodenum, the rectum and lung, during 1935, 1940 and 1945 to a million living males.

| Organ affected         | 1935 | 1940 | 1945 | Increase % during ten years |
|------------------------|------|------|------|-----------------------------|
| Stomach and duodenum.. | 349  | 409  | 465  | 33                          |
| Rectum .. .. .         | 164  | 194  | 238  | 45                          |
| Lung .. .. .           | 131  | 222  | 370  | 180                         |

There has been an increase of 180% from carcinoma of lung during the past ten years and the death-rate from the lung is now greater than that from the rectum and is approaching that of the stomach. The figure 180% has been criticized, but there is no doubt that there has been a significant increase.

The next point to consider is the present position of surgery in relation to carcinoma of the bronchus.

From a short survey of some of the literature it is difficult to decide what is at present the average operability. Some American authors quote an operability of 39%, but this high figure is considered by English writers to be due to a gross selection of cases. On the other hand, an operability of 1.4% was given by the British Empire Cancer Campaign in 1943. In 'Ludor Edwards' series, the rate was 7%. Recently Brock published the results of a series of 666 cases during the past seven years and found an average operability of 11% and he was encouraged to find the figure rising to 15% during the last three years. At the present time, therefore, the very best figure is 15%.

In the diagnosis, the history is usually far more important than the physical examination. Carcinoma of the bronchus may spread to the mediastinal glands before collapse, infection or the factors which give rise to physical signs appear. The history is therefore all-important in present medical practice and it is important for one thing only—it directs attention, or could do, towards radiography and other investigations.

In the diagnosis, Brock states that the sooner it is realized that by radiography alone can most cases be recognized reasonably early, the sooner will this dread disease become more treatable.

If radiography is so important, the question arises, "What part has mass radiography to play in the early recognition of this disease?"

To date, a total number of very nearly 400 cases has been discovered by mass radiography.

different localities, and these probably give a fair representation of the types of heart disease detected throughout the country as a whole.

#### INCIDENCE OF RHEUMATIC DISEASES

The returns over the three-year period consistently show the incidence of rheumatic heart disease to be 4 per 1,000. This figure is, of course, an underestimate because only those cases which show a considerable alteration in the shape or size of the heart are detected by mass radiography. We know that a large number of rheumatic hearts show no radiological abnormality and in some of the Units no return is made if the patient is aware that he or she has an abnormal heart. The correct rate for the groups examined is probably between 6 and 7 per 1,000. These figures amply confirm Parkinson's suggestion that there are over 200,000 people with rheumatic heart disease in this country. Indeed clinical data indicate that if we examined younger age-groups, this figure might well be doubled. There is little doubt that rheumatic heart disease is as big a social problem as pulmonary tuberculosis.

20% of the cases detected by mass radiography are unaware of any disability and have no history of rheumatic infection. It is noteworthy that the size of the heart has no bearing on this. One would have expected that a large heart, more prone to disorders of rhythm, would be unlikely to have escaped clinical observation, yet some of the largest hearts have been found in the symptomless groups.

In the larger of the two samples analysed (25,000) more than half the cases detected were over 40 years and 15% were over 50 years of age. The disease is more frequent in the lower income groups but in what proportion has not been assessed. The rate in an industrial city with a large slum area was found to be ten times greater than that in a neighbouring semi-urban area.

These gloomy figures stress the necessity for compulsory notification and the provision of suitable institutions for treatment of children with rheumatic disease. Tuberculosis is slowly but surely being brought under control while rheumatic heart disease may actually be increasing.

In the older age-groups, cardiac enlargement associated with hypertension is a fairly frequent finding and of course an occasional cardiac aneurysm is found. In a survey of a mental hospital with some 2,000 patients, the incidence of rheumatic heart disease was similar to that in the general population. There were in addition 8 patients with considerable cardiac enlargement. In only one of these, with myxœdema, could an ætiological factor be found.

Although we have no figures, most of the directors of the Units comment on the frequency with which they find aortic aneurysms and this is confirmed by the findings in the Central Unit. It is possible that many of these individuals die suddenly and are wrongly certified as dying from cardiac infarction.

#### CONGENITAL MALFORMATIONS

Mass radiography is bringing to light a large number of congenital malformations. Shortage of staff and lack of adequate follow-up facilities as the Units move about detract from the value of the available material, but there is unquestionably a wealth of material which it is hoped will be intensively studied under the new organization.

The most common and misleading congenital malformation is the funnel-chest deformity with cardiac displacement. The heart as a whole is displaced upwards and to the left, the pulmonary artery is prominent and the aortic knuckle small. There is often a dense opacity in the right cardiophrenic angle. This is partly a projection phenomenon through the depression and partly a result of angulation of the right lower lobe vein and artery. In many instances there is a steep downward declivity of the anterior ends of the ribs and this is an obvious pointer to the correct diagnosis. I estimate the incidence of this deformity at 1 in 300. It is of no significance except in severe cases, but unfortunately it is not infrequent to come across cases which have been previously diagnosed as organic heart disease. The anatomical opacity in the right cardiophrenic angle has also been mistaken for pneumonia and carcinoma.

#### COARCTATION OF AORTA

The most dramatic discovery, of course, is coarctation of the aorta. The incidence in the mass radiography groups is 1 in 80,000 but if we allow for errors and the absence of children under 15 from the surveys, the correct figure would be about 1 in 50,000.

The variety of the appearances and types of coarctation is astonishing. They range from the straightforward case with an obvious absence of the aortic knuckle to complex types with





The rate per 1,000 persons examined is about 0.20 for men and for women 0.03. The average age for men was 54 and for women 52.

The total number of cases discovered during 1948 was 170, and one Unit discovers about 7 cases a year.

It is of interest to know the incidence of this disease in the general public, but what is of greatest importance in any series of cases is surely the operability.

I have examined the figures of some Units, two of which have been operating for six years. The number of cases discovered was 55 and the incidence of this small series was 0.08 per 1,000.

There was a considerable variation in the operability.

One Unit discovered 12 cases of which 6 were operable. Another discovered 16 of which only 2 were operable. Of the 55 cases, 27% were operable. It is too early yet to place any reliance on these figures, but there is no doubt that by mass radiography the operability of bronchial carcinomata is being increased.

The time has now surely come to take more seriously the early trivial symptoms of respiratory tract disease and to state that, in the presence of such symptoms, no examination of the chest is complete without an X-ray film. It is now no longer safe to say to the man who complains of his smoker's cough, or his attack of bronchitis, that there is nothing seriously wrong because on clinical examination no physical signs of disease are found.

If we are to progress with early diagnosis of respiratory disease in the next ten years, two main problems must be overcome:

Firstly, patients rarely consult their doctors for trivial symptoms. The only answer to this is the extension of the facilities now offered by mass radiography until large sections of the population realize that regular chest X-rays are as much a personal and civic duty as visits to the dentist or going out to vote. Such a procedure would be an enormous and expensive undertaking and, if the facilities were provided, it is by no means certain that the public would use them. However, in view of the appallingly high incidence of pulmonary tuberculosis in the 18 to 25 age-groups, which we almost take for granted, such a course of action, at least for certain age-groups, needs earnest and careful consideration.

Secondly, most doctors do not feel justified in recommending a man for an X-ray who only has trivial symptoms. If, however, general practitioners realized that once a fortnight or perhaps even once a week mass miniature radiography facilities were available locally during the day and evening, then I am sure more people with early respiratory disease would have a chance of early diagnosis. Now that mobile X-ray vans are being produced such facilities are becoming practicable and possible.

In conclusion, I should like to say that with experience in reading miniature films for six to twelve months, the detection of abnormalities, if not their interpretation, is as sure on a miniature film as on a full-size film.

We have not yet exploited the full value of this technical achievement.



The rate per 1,000 persons examined is about 0.20 for men and for women 0.03. The average age for men was 54 and for women 52.

The total number of cases discovered during 1948 was 170, and one Unit discovers about 7 cases a year.

It is of interest to know the incidence of this disease in the general public, but what is of greatest importance in any series of cases is surely the operability.

I have examined the figures of some Units, two of which have been operating for six years. The number of cases discovered was 55 and the incidence of this small series was 0.08 per 1,000.

There was a considerable variation in the operability.

One Unit discovered 12 cases of which 6 were operable. Another discovered 16 of which only 2 were operable. Of the 55 cases, 27% were operable. It is too early yet to place any reliance on these figures, but there is no doubt that by mass radiography the operability of bronchial carcinomata is being increased.

The time has now surely come to take more seriously the early trivial symptoms of respiratory tract disease and to state that, in the presence of such symptoms, no examination of the chest is complete without an X-ray film. It is now no longer safe to say to the man who complains of his smoker's cough, or his attack of bronchitis, that there is nothing seriously wrong because on clinical examination no physical signs of disease are found.

If we are to progress with early diagnosis of respiratory disease in the next ten years, two main problems must be overcome:

Firstly, patients rarely consult their doctors for trivial symptoms. The only answer to this is the extension of the facilities now offered by mass radiography until large sections of the population realize that regular chest X-rays are as much a personal and civic duty as visits to the dentist or going out to vote. Such a procedure would be an enormous and expensive undertaking and, if the facilities were provided, it is by no means certain that the public would use them. However, in view of the appallingly high incidence of pulmonary tuberculosis in the 18 to 25 age-groups, which we almost take for granted, such a course of action, at least for certain age-groups, needs earnest and careful consideration.

Secondly, most doctors do not feel justified in recommending a man for an X-ray who only has trivial symptoms. If, however, general practitioners realized that once a fortnight or perhaps even once a week mass miniature radiography facilities were available locally during the day and evening, then I am sure more people with early respiratory disease would have a chance of early diagnosis. Now that mobile X-ray vans are being produced such facilities are becoming practicable and possible.

In conclusion, I should like to say that with experience in reading miniature films for six to twelve months, the detection of abnormalities, if not their interpretation, is as sure on a miniature film as on a full-size film.

We have not yet exploited the full value of this technical achievement.

